UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF PENNSYLVANIA

IN RE: TYLENOL (ACETAMINOPHEN) MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION	§	**MDL NO. 2436** **2:13-md-02436** **HON. LAWRENCE F. STENGEL**
This Document Relates to: Rana Terry, as Personal Representative and Administrator of the Estate of Denice Hayes, Deceased, Plaintiff, vs. McNEIL-PPC, Inc., McNeil Consumer Healthcare, and Johnson & Johnson, Inc., Defendants.	§	Civil Action No. 2:12-cv-07263

M E M O R A N D U M

Stengel, J. **November 13, 2015**

This case is part of a Multidistrict Litigation (MDL) involving claims of liver damage from the use of Tylenol at or just above the recommended dosage.[1] This is the

[1] See Master Compl., 13-md-2436, Doc. No. 32. There are close to two hundred other cases included in this MDL, along with several similar cases in New Jersey state court.

first "bellwether" scheduled for trial.[2] The plaintiff claims that her sister died of acute liver failure after taking Extra Strength Tylenol "as directed" by its label.[3] She asserts that defendants Johnson & Johnson and McNeil—the makers of Tylenol—knew or should have known that consumers may develop acute liver failure after taking Extra Strength Tylenol at or just above the recommended dose, yet failed to warn users of this risk.

The defendants moved for summary judgment on the plaintiff's failure-to-warn claim, arguing that the plaintiff has not offered sufficient evidence of this claim and/or the claim is preempted by federal law. For the reasons explained below, I will deny the defendants' motion.

I. A HISTORICAL OVERVIEW OF TYLENOL[4]

The plaintiff's claims are different from those previously asserted against the defendants about the safety of Tylenol. While previous cases have questioned whether Tylenol can cause liver damage, this case and others in this MDL question the extent of

[2] A "bellwether" case is a test case. "Bellwether" trials should produce representative verdicts and settlements. The parties can use these verdicts and settlements to gauge the strength of the common MDL claims to determine if a global resolution of the MDL is possible. See FEDERAL JUDICIAL CENTER, MANUAL FOR COMPLEX LITIGATION, FOURTH EDITION 360 (2004); DUKE LAW CENTER FOR JUDICIAL STUDIES, MDL STANDARDS AND BEST PRACTICES 16-21 (2014).

[3] See Compl., 12-cv-07263, Doc. No. 1.

[4] Some of the information offered by the plaintiff relates to events that happened after the decedent's death. Whether this information can be presented at trial will depend upon the outcome of a pending motion in limine and objections based on the Federal Rules of Evidence. I offer it here to provide a holistic picture of the background of Extra Strength Tylenol. Some of the information may be admissible or relevant in this case and/or subsequent cases in the MDL. In making my determinations about sufficiency of evidence, I do not rely solely on this evidence but offer it as potential evidence that, with other admissible evidence, could affect a jury's decision.

such damage and the quickness with which it can occur. A historical overview of the regulation and science of Tylenol is helpful in explaining the plaintiff's claims.

a. TYLENOL, ACETAMINOPHEN, AND LIVER DAMAGE[5]

Extra Strength Tylenol is an over-the-counter (OTC) pain reliever; consumers do not need a prescription to buy it. The active ingredient in Extra Strength Tylenol is acetaminophen, which is an analgesic and antipyretic or pain reliever and fever reducer.[6] Defendant McNeil manufactures and markets many different Tylenol products, including Extra Strength Tylenol and Regular Strength Tylenol. The two products differ in that one tablet of Extra Strength Tylenol contains 500 mg of acetaminophen while a tablet of Regular Strength Tylenol contains only 325 mg of acetaminophen per tablet. Johnson & Johnson is the parent company of McNeil and is involved in managing its operations.

Acetaminophen was first synthesized as a pain reliever in the 1890s and has been available OTC since the 1960s.[7] Tylenol is one of more than 600 acetaminophen-containing products on the market in the United States in OTC and prescription formulations.[8] Acetaminophen is one of the most widely used OTC drugs.[9] Twenty

[5] The defendants' exhibits can be found at Doc. No. 49. The plaintiff's exhibits have been filed under seal and are docketed at Doc. No. 90. Because a number of exhibits are under seal, my citations to exhibits in this motion note if they are the defendants' or the plaintiff's and do not necessarily offer a specific docket cite.

[6] E.g., http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm165107.htm (last visited October 15, 2015).

[7] See, e.g., FDA Memorandum, Aug. 15, 2002 (Pl. Ex. 17); Lee, W.M., Acetaminophen Toxicity: Changing Perceptions on a Social/Medical Issue, Hepatology 46(4): 966-970 (2007)(Pl. Ex. 9).

[8] http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm336581.htm (last visited Oct. 13, 2015).

[9] See Kaufman DW, et al., Recent patterns of medication use in the ambulatory adult population of the United States: the Slone Survey, J. Am. Med. Assoc. (2002), 287:337-44 (Def. Ex. A, Doc. No. 49-1); Slone Epidemiological Center at Boston University, Patterns of Medications Use in the United States 2005: A Report from

percent of Americans—60 million people—ingest an acetaminophen-containing product each week.[10] The Food and Drug Administration (FDA), which regulates OTC drugs, has found acetaminophen to be a "safe and effective OTC analgesic" when taken in recommended doses and used according to the label.[11] However, acetaminophen has been known to cause severe liver damage.[12]

i. Acetaminophen's Link to Acute Liver Failure

Acetaminophen is different from other OTC pain relievers in two ways: 1) it is the only one to have an antidote, and 2) its maximum total daily limit is the same for both OTC and prescription products.[13] Acetaminophen is a "dose-related toxin," meaning it can be safely used at certain doses but harmful at higher doses.[14] As a result, there is evidence that it has a "narrow therapeutic margin"—i.e., there is little difference

---

the Slone Survey, *available at* http://www.bu.edu/slone/research/studies/slone-survey (last visited October 13, 2015).

[10] Kaufman DW, et al., Recent patterns of medication use in the ambulatory adult population of the United States: the Slone Survey, J. Am. Med. Assoc. (2002), 287:337-44 (Def. Ex. A, Doc. No. 49-1); Slone Epidemiological Center at Boston University, Patterns of Medications Use in the United States 2005: A Report from the Slone Survey, *available at* http://www.bu.edu/slone/research/studies/slone-survey (last visited Oct. 13, 2015).

[11] See Defendants' Statement of Facts at ¶ 9; Plaintiff's Statement admitting this fact; 42 Fed. Reg. 35346, 35413 (Jul. 8, 1977)(Def. Ex. B, Doc. No. 49-2).

[12] See 42 Fed. Reg. 35356, 35447 (Jul. 8, 1977); Lee, et. al., MEETING REPORT: Acute Liver Failure: Summary of a Workshop, Hepatology 2008; 47:1401-1415 (Pl. Ex. 6); Larson, et. al., Acetaminophen-Induced Acute Liver Failure: Results of a United States Multicenter, Prospective Study, Hepatology 2005; 42(6):1364-1372 (Pl. Ex. 7); Lee, W.M., Acetaminophen Toxicity: Changing Perceptions on a Social/Medical Issue, Hepatology 46(4): 966-970 (2007)(Pl. Ex. 9).

[13] See CDER Working Group Executive Summary and Recommendations, Feb. 26, 2008 (Pl. Ex. 8).

[14] See Lee, et. al. MEETING REPORT: Acute Liver Failure: Summary of a Workshop, Hepatology 2008; 47:1401-1415 (Pl. Ex. 6).

between the current maximum recommended dose of acetaminophen and the doses that could cause liver injury.[15] The parties debate how narrow this margin is.

A simplistic explanation of how the body metabolizes acetaminophen helps frame the issues in this case. Typically, glutathione—an antioxidant found in the liver—will bind to the toxic parts of acetaminophen, to neutralize them and prevent them from harming the body.[16] These neutralized toxins are then excreted.[17] However, if the body does not have enough glutathione, those toxins can build up in the liver, causing acute liver failure (ALF). Glutathione stores may be low when a person is malnourished or when the liver has been neutralizing a lot of toxins at once.[18]

"Acute liver failure (ALF) is a rapid deterioration of the organ's ability to function."[19] Patients who experience ALF can fall into a coma or die.[20] They may require a

[15] See, e.g., CDER Working Group Executive Summary and Recommendations, Feb. 26, 2008 (Pl. Ex. 8)("Acetaminophen has a narrow therapeutic margin, that is, there is little difference between the current maximum recommended dose of acetaminophen and the doses that are associated with a potentially elevated risk of hepatotoxicity."); AASLD Memo, Apr. 27, 2007 (Pl. Ex. 19); Christina Chang, M.D., M.P.H., Division of Nonprescription Clinical Evaluation, Office of Nonprescription Products of the FDA, Powerpoint, Jun. 29, 2009 (Pl. Ex. 21).

[16] See Lee, et. al. MEETING REPORT: Acute Liver Failure: Summary of a Workshop, Hepatology 2008; 47:1401-1415 (Pl. Ex. 6); Whitcomb & Block, Association of Acetaminophen Hepatotoxicity with Fasting and Ethanol Use, 272 JAMA 23, 1845-1850 (1994)(Pl. Ex. 12).

[17] See 42 Fed. Reg. 35381 (Jul. 8, 1977)(explaining studies of acetaminophen's effect on the liver)("The administration of acetaminophen to patients with impaired renal function results in increased accumulation of acetaminophen conjugates in the plasma because of poor excretory capacity but only in minor changes in the plasma concentrations of free acetaminophen.").

[18] See 74 Fed. Reg. 19397 (Apr. 29, 2009)("Malnourished individuals have been shown to have reduced glutathione levels."); 63 Fed. Reg. 56796-02 (Oct. 23, 1998)("In addition to dosage, hepatotoxicity due to acetaminophen use is also dependent on factors such as liver glutathione stores, nutritional state, age, and in some cases, chronicity of usage.").

[19] FDA, Some Drugs and the Liver Don't Mix, May 2014 (Def. Ex. E, Doc. No. 49-5).

[20] See Lee, et. al. MEETING REPORT: Acute Liver Failure: Summary of a Workshop, Hepatology 2008; 47:1401-1415 (Pl. Ex. 6); FDA Memorandum, Aug. 15, 2002 (Pl. Ex. 17); Characterization of Acetaminophen Overdose and

liver transplant.[21] A person who has recovered from ALF may still be at risk of redeveloping it, if the person again consumes too much acetaminophen.[22]

If acetaminophen-induced ALF is recognized quickly, acetaminophen's antidote (*N*-acetylcysteine or NAC) can be given to a patient to supply glutathione and prevent or decrease liver injury.[23] However, persons who have developed ALF from an unintentional acetaminophen overdose may not realize their liver injury because symptoms of ALF are not readily apparent or may look like the symptoms the acetaminophen is being used to treat (i.e., flu symptoms). [24]

ii. FDA Actions to Address Acetaminophen-Induced Acute Liver Failure

The majority of acute liver failure cases in the United States are related to the use of acetaminophen.[25] Each year, acetaminophen is responsible for hundreds of deaths and

---

Related Hepatotoxic Events, Joint Meeting of the Drug Safety and Risk Management, Nonprescription and Anesthetic and Life Support Drugs Advisory Committees of the FDA, Powerpoint, Jun. 29, 2009 (Pl. Ex. 21).

[21] See Lee, et. al. MEETING REPORT: Acute Liver Failure: Summary of a Workshop, Hepatology 2008; 47:1401-1415 (Pl. Ex. 6).

[22] See Lee, et. al. MEETING REPORT: Acute Liver Failure: Summary of a Workshop, Hepatology 2008; 47:1401-1415 (Pl. Ex. 6).

[23] See Lee, et. al. MEETING REPORT: Acute Liver Failure: Summary of a Workshop, Hepatology 2008; 47:1401-1415 (Pl. Ex. 6); Larson, et. al., Acetaminophen-Induced Acute Liver Failure: Results of a United States Multicenter, Prospective Study, Hepatology 2005; 42(6):1364-1372 (Pl. Ex. 7); Lee, W.M., Acetaminophen Toxicity: Changing Perceptions on a Social/Medical Issue, Hepatology 46(4): 966-970 (2007)(Pl. Ex. 9).

[24] 42 Fed. Reg. 35356 (Jul. 8, 1977). See also CDER Working Group Executive Summary and Recommendations, Feb. 26, 2008 (Pl. Ex. 8)("The symptoms of acetaminophen overdose may not appear for up to three days, so people may continue to take acetaminophen and increase the damage. The symptoms of liver injury may mimic the condition that they are treating (e.g., flu symptoms).").

[25] See FDA, Some Drugs and the Liver Don't Mix, May 2014 (Def. Ex. E, Doc. No. 49-5); Lee, et. al. MEETING REPORT: Acute Liver Failure: Summary of a Workshop, Hepatology 2008; 47:1401-1415 (Pl. Ex. 6). See also Larson, et. al., Acetaminophen-Induced Acute Liver Failure: Results of a United States Multicenter, Prospective Study, Hepatology 2005; 42(6):1364-1372 (Pl. Ex. 7); Gerald Dal Pan, M.D., Director of Office of Surveillance and Epidemiology, CDER/FDA, Powerpoint, Jun. 29, 2009 (Pl. Ex. 21).

liver transplants, in addition to tens of thousands of hospitalizations.[26] These acetaminophen-induced liver injury patients include both people who are intentionally trying to harm themselves (i.e., attempting suicide) and those who take acetaminophen for therapeutic reasons (i.e., to treat physical pain).[27] There is evidence that patients taking acetaminophen at 4 g per day—the recommended maximum daily dose until recently—may be at risk of developing acute liver failure.[28]

Medical literature began questioning the safety of acetaminophen at or just above therapeutic levels as far back as the 1980s.[29] During the 1990s, members of the medical community continued to raise concerns about acute liver failure occurring in patients at or even lower than the maximum daily dose of 4 grams.[30] Throughout this same time period, McNeil was also actively engaged in research and development of a drug or

[26] See FDA Background Package for June 29-30, 2009 Advisory Committee Meeting (Pl. Ex. 8); FDA Safety Analysis Power Point, Sept. 19, 2002 (Pl. Ex. 11). See also Lee, W.M., Acetaminophen Toxicity: Changing Perceptions on a Social/Medical Issue, Hepatology 46(4): 966-970 (2007)(Pl. Ex. 9); FDA Memorandum, Aug. 15, 2002 (Pl. Ex. 17).

[27] See FDA Background Package for Jun. 29-30, 2009 Advisory Committee Meeting (Pl. Ex. 8); FDA Safety Analysis Power Point, September 19, 2002 (Pl. Ex. 11); Lee, W.M., Acetaminophen Toxicity: Changing Perceptions on a Social/Medical Issue, Hepatology 46(4): 966-970 (2007)(Pl. Ex. 9); FDA Safety Analysis Power Point, Sept. 19, 2002 (Pl. Ex. 11); FDA Memorandum, Aug. 15, 2002 (Pl. Ex. 17); Gerald Dal Pan, M.D., Director of Office of Surveillance and Epidemiology, CDER/FDA, Powerpoint, Jun. 29, 2009 (Pl. Ex. 21); Characterization of Acetaminophen Overdose and Related Hepatotoxic Events, Joint Meeting of the Drug Safety and Risk Management, Nonprescription and Anesthetic and Life Support Drugs Advisory Committees of the FDA, Powerpoint, Jun. 29, 2009 (Pl. Ex. 21).

[28] See 71 Fed. Reg. 77314 (Dec. 26, 2006)(Pl. Ex. 10); Larson, et. al., Acetaminophen-Induced Acute Liver Failure: Results of a United States Multicenter, Prospective Study, Hepatology 2005; 42(6):1364-1372 (Pl. Ex. 7); FDA Safety Analysis Power Point, Sept. 19, 2002 (Pl. Ex. 11). See also CDER Working Group Executive Summary and Recommendations, Feb. 26, 2008 (Pl. Ex. 8).

[29] There is also evidence the McNeil executives were aware of this medical literature. See McNeil Memorandum, Nov. 19, 1987 (Pl. Ex. 14); P. Gussin Dep., Dec. 12, 2013 at 198 (Pl. Ex. 15).

[30] See Erikkson, L.S., et al., Hepatotoxicity due to repeated intake of low doses of paracetamol, J Intern Med, 1992: 231:567-570 (Pl. Ex. 16).

combination of ingredients that would reduce or eliminate acetaminophen's potentially toxic effects on the liver.[31]

In 2002, the FDA convened an Advisory Committee to discuss ways to prevent liver injury caused by unintentional acetaminophen overdose.[32] During the Committee Meeting, the FDA presented findings from medical literature: 1) that hepatotoxicity may occur "at recommended doses of APAP," 2) that such cases were linked to risk factors such as alcohol use and/or fasting, and 3) that some cases of unintentional overdose led to death.[33] The FDA also presented its own findings from a review of its own internal Adverse Event Reporting (AER) database. The FDA found hepatotoxicity (i.e., liver damage) in persons who have ingested less than 4 grams/day and who had risk factors like alcohol and "poor nutritional status."[34] As a result, the American Association of the Study of Liver Disease (AASLD) and the FDA offered specific recommendations for enhancing safety warnings and instructions for acetaminophen-based products.[35]

In 2006, the FDA proposed a rule to strengthen warnings regarding the risk of liver damage from taking acetaminophen. After receiving and reviewing public

[31] The plaintiff brings a separate design defect claim. I address the merits of that claim in a separate decision regarding a motion for summary judgment on that claim.

[32] See FDA Safety Analysis Power Point, Sept. 19, 2002 (Pl. Ex. 11); FDA Memorandum, Aug. 15, 2002 (Pl. Ex. 17).

[33] See FDA Safety Analysis (Pl. Ex. 11). See also Larson, et. al., Acetaminophen-Induced Acute Liver Failure: Results of a United States Multicenter, Prospective Study, Hepatology 2005; 42(6):1364-1372 (Pl. Ex. 7)(explaining how fasting may enhance toxicity and how unintentional "overdose" seemed possible at recommended dosing levels).

[34] See FDA Safety Analysis at Slide 44 (Pl. Ex. 11). This data was later published in the Federal Register as part of FDA's Proposed Rule for the 2009 Label Change, discussed below. See 71 Fed. Reg. 77314 (Dec. 26, 2006)(Pl. Ex. 10).

[35] See FDA Background Package (Pl. Ex. 8); AASLD Memo, Apr. 27, 2007 (Pl. Ex. 19).

comments, the FDA promulgated a final rule outlining the liver warnings it found to be necessary. [36] This final rule, issued in 2009, is explained further below.

In February 2008, the Acetaminophen Hepatotoxicity Working Group for the Center for Drug Evaluation and Research of the FDA met to discuss ways to address unintentional acetaminophen overdose.[37] The Group outlined several recommendations, including a reduction in the maximum tablet strength from 500 mg to 325 mg.[38] The reduction in tablet strength was intended to reduce the overall recommended daily dose of Tylenol from 4,000 mg to 3,250 mg.[39] This recommendation was made over the objection of an unnamed acetaminophen manufacturer which asserted the data did not support a need for the change; the Group looked at Adverse Events Reports (AERs) showing that daily doses of 4 g presented a risk for some individuals.[40] Survey data also showed that "people routinely and knowingly take more than the recommended dose of OTC pain relievers."[41]

In June 2009, a joint meeting of several FDA Advisory Committees was held to discuss the issue of liver injury related to acetaminophen use.[42] The joint committee

---

[36] See also Gerald Dal Pan, M.D., Director of Office of Surveillance and Epidemiology, CDER/FDA, Powerpoint, Jun. 29, 2009 (Pl. Ex. 21)(offering the history of the FDA's efforts to address unintentional acetaminophen-induced ALF).

[37] CDER Working Group Executive Summary and Recommendations, Feb. 26, 2008 (Pl. Ex. 8).

[38] CDER Working Group Executive Summary and Recommendations, Feb. 26, 2008 (Pl. Ex. 8).

[39] CDER Working Group Executive Summary and Recommendations, Feb. 26, 2008 (Pl. Ex. 8).

[40] See CDER Working Group Executive Summary and Recommendations, Feb. 26, 2008 (Pl. Ex. 8).

[41] CDER Working Group Executive Summary and Recommendations, Feb. 26, 2008 (Pl. Ex. 8).

[42] See McNeil Powerpoint (Pl. Ex. 22). This meeting is discussed in more detail in the decision regarding the defendants' motion for summary judgment on the plaintiff's design defect claim.

recommended that the warning on acetaminophen products be further strengthened and the recommended dose reduced.[43]

b. THE REGULATORY FRAMEWORK FOR TYLENOL

OTC drugs are approved by the FDA through two separate routes: the New Drug Application (NDA) process and the monograph system.[44] During the forty or so years Extra Strength Tylenol has been available OTC, it has been regulated under both FDA regulatory processes.

i. New Drug Application v. Monograph Process

The NDA process requires specific products be approved for sale with specific labeling. [45] The monograph system allows for the marketing of OTC drugs containing

---

[43] See, e.g., FDA Press Releases, FDA limits acetaminophen in prescription combination products; requires liver toxicity warnings, Jan. 13, 2011, *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm239894.htm ("An FDA advisory committee discussed the issue at a meeting in June, 2009, and recommended strengthening the warning about severe liver injury on the drug labels of prescription products containing acetaminophen.").

[44] E.g., "How Drugs are Developed and Approved – OTC (Nonprescription) Drugs," http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ucm209647.htm; "How Drugs are Developed and Approved – Over-the-Counter (OTC) Drug Monograph Process," http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedand Approved/ucm317137.htm; Gerald Dal Pan, M.D., Director of Office of Surveillance and Epidemiology, CDER/FDA, Powerpoint, Jun. 29, 2009 (Pl. Ex. 21).

A detailed recitation of the regulatory process and history is also included in the Declaration of Judith Jones, Ph.D. (May 20, 2015)(Def. Ex. S, 49-19 to 49-28), FDA/CDER, Guidance for FDA Staff and Industry, Marketed Unapproved Drugs—Compliance Policy Guide, Sec. 440.100 Marketed New Drugs Without Approved NDAs or ANDAs, Sep. 19, 2011 (Doc. 49-20)(Ex. C attached to J. Jones Report, Def. Ex. S), the expert report of Cheryl Blume, Ph.D. (May 5, 2014)(Pl. Ex. 26), and the Affidavit of Gerald Rachanow, Esq. (Pl. Ex. 25). All three experts—Jones (for the defendants) and Blume and Rachanow (for the plaintiff)—have offered expert opinions about the FDA's regulatory process. Each side has filed a Daubert motion to exclude the other's opinion(s); these Daubert motions are still pending.

[45] E.g., "How Drugs are Developed and Approved – OTC (Nonprescription) Drugs," http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ucm209647.htm; "How Drugs are Developed and Approved – Over-the-Counter (OTC) Drug Monograph Process," http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedand Approved/ucm317137.htm. A detailed recitation of the regulatory process and history is included in the

particular ingredients, which were already on the market before the FDA established the monograph system in 1972.[46] These active ingredients, which include acetaminophen, were ones which had been found to be generally safe and effective through general usage.[47] Therefore, they were allowed to remain on the market OTC.

Because Extra Strength Tylenol's active ingredient is acetaminophen, it was automatically regulated by the monograph system as of 1972. In 1975, the FDA approved Extra Strength Tylenol as "safe and effective for use as recommended in the submitted labeling," pursuant to a New Drug Application (NDA 17-552).[48] In the FDA's letter approving Extra Strength Tylenol for OTC sale and use under the NDA, the FDA also noted that "upon publication in the FEDERAL REGISTER of the OTC Monograph for

---

Declaration of Judith Jones, Ph.D. (May 20, 2015)(Jones Decl.)(Doc. No. 49, Def. Ex. S (and exhibits attached thereto)).

See also Mut. Pharm. Co., Inc. v. Bartlett, – U.S. –, 133 S. Ct. 2466, 2470-71 (2013)("An NDA is a compilation of materials that must include 'full reports of [all clinical] investigations,' § 355(b)(1)(A), relevant nonclinical studies, and 'any other data or information relevant to an evaluation of the safety and effectiveness of the drug product obtained or otherwise received by the applicant from any source,' 21 C.F.R. §§ 314.50(d)(2) and (5)(iv) (2012). The NDA must also include 'the labeling proposed to be used for such drug,' 21 U.S.C. § 355(b)(1)(F); 21 C.F.R. § 314.50(c)(2)(i), and 'a discussion of why the [drug's] benefits exceed the risks under the conditions stated in the labeling,' 21 C.F.R. § 314.50(d)(5)(viii); § 314.50(c)(2)(ix). The FDA may approve an NDA only if it determines that the drug in question is 'safe for use' under 'the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof.' 21 U.S.C. § 355(d)."); In re: Fosamax, 751 F.3d 150, 159 (3d Cir. 2014)("Under the FDCA, a manufacturer must seek approval from the United States Food and Drug Administration ('FDA') to market a new drug and, in doing so, must first file a New Drug Application ('NDA') and then prove the drug's safety and efficacy and propose accurate and adequate labeling. 21 U.S.C. § 355(b)(1), (d)."); In re: Celexa and Lexapro Marketing & Sales Pracs. Litig., 779 F.3d 34, 35-36 (1st Cir. 2015).

[46] See "How Drugs are Developed and Approved – Over-the-Counter (OTC) Drug Monograph Process," http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedand Approved/ucm317137.htm.

[47] E.g., "How Drugs are Developed and Approved – OTC (Nonprescription) Drugs," http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ucm209 647.htm; "How Drugs are Developed and Approved – Over-the-Counter (OTC) Drug Monograph Process," http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedand Approved/ucm317137.htm.

[48] FDA Approval letter (Hewes Decl. at Ex. 1)(Def. Ex. F, Doc. No. 49-6). See also Defendants' Statement of Material Facts, Material Fact No. 10; Plaintiff's Statement admitting fact.

acetaminophen, revision of the labeling or other action affecting the marketing of [Extra Strength Tylenol] may be required."[49] In 1998, McNeil voluntarily withdrew the NDA for Extra Strength Tylenol.[50] Since that time, Extra Strength Tylenol has been marketed pursuant to the monograph system only.[51]

The monograph system is essentially an expanded version of administrative notice-and-comment rulemaking, which required two rounds of proposals and comments as opposed to just one. The monograph process includes four main steps: 1) a review by panels of qualified experts which then recommend the conditions under which the drug can be used, 2) publication of a the expert panel's recommendations as a proposed rule in the Federal Register for public comment on safety and effectiveness, 3) FDA review of the comments on the experts' proposed rule and publication of a tentative final monograph (TFM) with a second opportunity for comments on the TFM, and 4) publication of the final monograph which includes the FDA's findings on when a drug is considered to be generally safe and effective for use.[52] See 21 C.F.R. § 330.10. A drug is considered "safe" under the monograph system when it has "a low incidence of adverse reactions or significant side effects under adequate directions for use and warnings

[49] FDA Approval letter (Hewes Decl. at Ex. 1)(Def. Ex. F, Doc. No. 49-6).

[50] Jones Decl., Doc. No. 49, Ex. S and Exs. T-U attached to Jones Decl. (May 1998 communications from McNeil requesting withdrawal of approved NDA, and FDA letter in response acknowledging withdrawal).

[51] Jones Decl., Doc. No. 49, Ex. S and Ex. T attached to Jones Decl. (McNeil letter withdrawing NDA)("We intend to continue to market Extra Strength TYLENOL® Tablets as an OTC monograph product and will continue to submit acetaminophen Adverse Drug Experience reports under NDA 19-872.").

[52] See also Gerald Dal Pan, M.D., Director of Office of Surveillance and Epidemiology, CDER/FDA, Powerpoint, Jun. 29, 2009 (Pl. Ex. 21).

against unsafe use as well as low potential for harm which may result from abuse under conditions of widespread availability." 21 C.F.R. § 330.10(a)(4).

ii. Regulation of Acetaminophen Under the Monograph System

In 1972, acetaminophen was listed as "an effective analgesic" under the Drug Efficacy Study Implementation program implemented by the FDA, which was the first phase of what would become the monograph process.[53] In 1977, the FDA published a Proposed Rule for Internal Analgesic, Antipyretic, and Antirheumatic (IAAA) Products reflecting the Advisory Panel's report on this category of ingredients.[54] This Rule categorized acetaminophen as a Category I active ingredient, meaning that it was "generally recognized as safe and effective" or GRASE. That proposed rule made clear that warnings on products containing those ingredients were still important: "[b]ecause OTC products can be purchased by anyone [and] the public generally does not regard those products as medicines which, if used improperly, can result in injurious or potentially serious consequences."[55] The rule explained: "The consumer should be informed of any possible signs of known toxicity or any indication requiring discontinuation of the use of the drug so that appropriate steps may be taken before more severe symptoms become apparent."[56] Specifically, the Proposed Rule noted: "acetaminophen has no [] sign of toxicity or 'safety valve' to alert the consumer [to the

[53] Fed. Reg. 7820 (Apr. 20, 1972)(Doc. No. 49, Ex. T).

[54] 42 Fed. Reg. 35346 (Jul. 8, 1977)(Pl. Ex. B attached to Ex. 3 (Affidavit of Gerald Rachanow, Esq.)) and (Def. Ex. I attached to Ex. S (Certification of Judith Jones, M.D., Ph.D.)).

[55] 42 Fed. Reg. 35355 (Jul. 8, 1977).

[56] 42 Fed. Reg. 35355 (Jul. 8, 1977).

development of ALF]."[57] For this reason, the Proposed Rule recommended that all products containing acetaminophen contain the warning, "Do not exceed recommended dosage because severe liver damage may occur."[58] The Proposed Rule also stated that a single dose of acetaminophen (2 tablets) containing 500 mg—i.e., Extra Strength Tylenol—should be taken every 6 hours while a single dose of 325 mg tablets could be taken every 4 hours.[59]

On November 16, 1988, the FDA issued a Tentative Final Monograph (TFM) for Internal Analgesic, Antipyretic, and Antirheumatic (IAAA) products, including acetaminophen.[60] In the TFM, the FDA reviewed comments on the 1977 Proposed Rule and determined which parts remained valid and which it declined to adopt. Though the FDA made its recommendations for regulating IAAA products, the TFM was still considered a proposed regulation subject to additional comments.[61] In the TFM, the FDA

[57] 42 Fed. Reg. 35356 (Jul. 8, 1977). See also CDER Working Group Executive Summary and Recommendations, Feb. 26, 2008 (Pl. Ex. 8)("The symptoms of acetaminophen overdose may not appear for up to three days, so people may continue to take acetaminophen and increase the damage. The symptoms of liver injury may mimic the condition that they are treating (e.g., flu symptoms)."); FDA, Some Drugs and the Liver Don't Mix, May 2014 (Def. Ex. E, Doc. No. 49-5)(describing symptoms of liver problems as fatigue, jaundice, and itchiness of the skin).

[58] 42 Fed. Reg. 35356, 35447 (Jul. 8, 1977). The Proposed Rule also noted that acetaminophen advertising may indicate that it is a safer product, when in fact, it may not be under certain circumstances. See id. The Rule went further: "Because the consumer needs to be correctly and fully informed, the Panel recommends that the advertising in any medium for these drugs that in any way uses the labeling, package or container not be inconsistent, even in subtle implication through mood, focus or innuendo, with the applicable labeling in the OTC internal analgesic monograph." Id. Though the Proposed Rule recognized that the FTC regulated commercial advertising, it "strongly urge[d] the [FTC] to require that the cautionary language and warnings developed by the Panel be given emphasis in commercial advertising more so than is currently being done…" Id.

[59] See 42 Fed. Reg. 35358 (Jul. 8, 1977)(chart).

[60] 53 Fed. Reg. 46204, 46248 (Nov. 16, 1988).

[61] See 21 C.F.R. §§ 310, 343, 369, 53 Fed. Reg. 46204, 46248, 46254 (Nov. 16, 1988)(TFM)(Pl's Ex. 48; Ex. C attached to Ex. 3 (Affidavit of Gerald Rachanow, Esq.)) or (Def. Ex.J attached to Ex. S (Certification of Judith Jones, M.D., Ph.D.)); FDA Letter re: FOIA request, Nov. 17, 2011 (Pl. Ex. 4).

continued to categorize acetaminophen under Category I: GRASE.[62] It adopted the Panel's recommended dosing as well.[63] Specifically, products containing acetaminophen were expected to have the following dosing instructions for adults: "325 to 650 milligrams every 4 hours or 325 to 650 milligrams every 3 hours or 650 to 1,000 milligrams every 6 hours, while symptoms persist, not to exceed 4,000 milligrams in 24 hours or as directed by a doctor."[64] It also "tentatively decided not to adopt the liver warning recommended by the Panel" though the FDA was "aware that liver damage can occur from acetaminophen overdosage."[65]

The FDA has not yet issued a Final Monograph for IAAA products. These products, including those containing acetaminophen, continue to operate under the Tentative Final Monograph (TFM). During the relevant timeframe of this case, Extra Strength Tylenol was only regulated by the TFM.[66] The FDA has explained: "Under a TFM, manufacturers market products at their own risk and are able to make voluntary adjustments [to their product's label] taking into account the information presented in the proposed TFM."[67] Until that final regulatory determination is made—if it ever is—the defendants remain responsible for all aspects of the Tylenol label.[68]

---

[62] 53 Fed. Reg. 46249 (Nov. 16, 1988).

[63] 53 Fed. Reg. 46251 (Nov. 16, 1988).

[64] 53 Fed. Reg. 46257 (Nov. 16, 1988).

[65] 53 Fed. Reg. 46214, 46252 (Nov. 16, 1988).

[66] See FDA Letter re: FOIA request, Nov. 17, 2011 (Pl. Ex. 4).

[67] See FDA Letter re: FOIA request, Nov. 17, 2011 (Pl. Ex. 4). See also E. Kuffner Dep., March 18, 2011 at 8-10 (Pl. Ex. 5)(explaining what duties a drug manufacturer has when new risks come to light in post-market surveillance); Wyeth v. Levine, 555 U.S. 555, 570-71 (2009)("[I]t has remained a central premise of federal drug

c. EXTRA STRENGTH TYLENOL LABELING FROM 1977 TO 2010

From 1977 until 1994, the label on Extra Strength Tylenol bottles remained virtually unchanged. Over the next ten years, McNeil petitioned the FDA three times to allow them to add additional warnings to the Extra Strength Tylenol label. In 1994, McNeil sought approval from the FDA to add a warning that taking Extra Strength Tylenol with alcohol or other products containing acetaminophen could cause liver damage.[69] The FDA approved this request.[70] During the approval process, the FDA informed McNeil that the Extra Strength Tylenol label was not in conformity with the TFM because it instructed consumers to take 2 caplets "every 4-6 hours" as opposed to every 6 hours.[71] In 1998, the FDA promulgated a final rule requiring that an alcohol warning be included on all acetaminophen products.[72]

---

regulation that the manufacturer bears responsibility for the content of its label at all times.")(discussed further below).

[68] See McNeil letter to the FDA re: label change, Jan. 27, 1995 (Def. Ex. Q attached to Ex. S (Certification of Judith Jones, M.D., Ph.D.))("We believe that the language we are using in the Directions section of our labeling is acceptable since the issue has not yet been finalized in the final monograph for Internal Analgesic Products.")(debating FDA's recommendation that language in McNeil's label be changed to conform to the TFM language on dosing).

[69] FDA Letter from McNeil, Jun 16, 1994 (Hewes Decl. at Ex. 2)(Def. Ex. F, Doc. No. 49-6); July 28, 1994 record of contact with FDA. (Hewes Decl. at Ex. 3)(Def. Ex. F, Doc. No. 49-6). See also Letter to Doctors regarding Alcohol Label Change (Pl. Ex. 49)("That's why, when the Food and Drug Administration Advisory Committees recommended that all over-the-counter pain relievers carry a warning on the label about the use of these medications and alcohol, the makers of TYLENOL were the first to voluntarily comply.").

[70] This label change was requested four years prior to the FDA's mandatory requirement that all acetaminophen products contain such language. FDA Letter from McNeil, Jun 16, 1994 (Hewes Decl. at Ex. 2)(Def. Ex. F, Doc. No. 49-6); McNeil Record of contact with FDA, Jul. 28, 1994 (Hewes Decl. at Ex. 3)(Def. Ex. F, Doc. No. 49-6). This change was requested for NDA 17-552.

[71] See FDA Letter/Fax to McNeil, Nov. 23, 1994 (Pl. Ex. E attached to Ex. 3 (Affidavit of Gerald Rachanow, Esq.)); FDA Letter to McNeil, Mar. 31, 1997 (Ex. F attached to Ex. 3 (Affidavit of Gerald Rachanow, Esq.)). McNeil did not agree with the FDA's determination. See McNeil letter to the FDA re: label change, Jan. 27, 1995 (Def. Ex. Q attached to Ex. S (Certification of Judith Jones, M.D., Ph.D.))("We believe that the language we are using in the Directions section of our labeling is acceptable since the issue has not yet been finalized in the final monograph for Internal Analgesic Products.").

In 2001, McNeil again petitioned the FDA to add a warning stating: "[t]aking more than the recommended dose (overdose) could cause serious health problems."[73] After an advisory committee meeting with the FDA about acetaminophen labeling and safety, McNeil submitted a second request to further strengthen its proposed warning change by replacing "serious health problems" language with specific language warning of overdose and liver damage.[74] The FDA approved that change in 2003.[75] In 2004, McNeil introduced a Tylenol warning that contained the following overdose/organ-specific liver damage language:

> Taking more than the recommended dose (overdose) may cause liver damage. In case of overdose, get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.[76]

In 2006, the FDA proposed new organ-specific warnings for all OTC internal

---

The FDA again sent a letter stating that the label dosing at 4 to 6 hours was not in compliance with the TFM. See FDA Letter to McNeil, Mar. 31, 1997 (Def. Ex. R attached to Ex. S (Certification of Judith Jones, M.D., Ph.D.))("The dosage recommendations are not consistent with the tentative final monograph or supported in the application. The second sentence should be revised to read, "Take two tablets every 6 hours."). On July 21, 1997, the FDA sent a letter to McNeil saying not to implement any of the changes in the previous 7- until the FDA has instructed them to. See Def. Ex. S attached to Ex. S (Certification of Judith Jones, M.D., Ph.D.).

Because the TFM is only a proposed rule not a final one, McNeil's decision to provide different dosing instruction would not be *per se* negligence. However, McNeil's decision to intentionally label Extra Strength Tylenol with instructions that could cause a person to consume more than the TFM's daily recommended dose is evidence that could lead a reasonable jury to believe that McNeil breached its duty to adequately warn the consumer of potential risks.

[72] See 63 Fed. Reg. 56789-02 (Oct. 23, 1998); Gerald Dal Pan, M.D., Director of Office of Surveillance and Epidemiology, CDER/FDA, Powerpoint, Jun. 29, 2009 (Pl. Ex. 21).

[73] McNeil Letter to FDA, Nov. 29, 2001 (Hewes Decl. at Ex. 4)(Def. Ex. F, Doc. No. 49-6).

[74] McNeil Letter to FDA, Oct 15, 2002 (Hewes Decl. at Ex. 5)(Def. Ex. F, Doc. No. 49-6).

[75] FDA letter to McNeil, May 28, 2003 (Hewes Decl. at Ex. 6)(Def. Ex. F, Doc. No. 49-6)(approving the changes "for use as recommended in the agreed upon labeling text").

[76] McNeil Letter to FDA, May 22, 2003 (Hewes Decl. at Ex. 7)(Def. Ex. F, Doc. No. 49-6).

analgesic, antipyretic, and antirheumatic (IAAA) drug products—including acetaminophen.[77] Using the notice and comment procedure found in the Administrative Procedures Act, the FDA put forth a proposed rule about the warnings, allowed for public comment, and then issued a "Final Rule" on April 29, 2009.[78] This "Final Rule" set the minimum requirements for acetaminophen labeling regarding liver damage warnings.[79] The 2009 Final Rule was designed "to inform consumers about the risk of liver injury when using acetaminophen."[80] The 2009 Final Rule is codified at 21 C.F.R. § 201.326.[81]

The 2009 Final Rule requires that all OTC products containing acetaminophen must include the following language on their label:

> Liver warning [heading in bold type]: This product contains acetaminophen.
>
> Severe liver damage may occur if you take [bullet] more than [insert maximum number of daily dosage units] in 24 hours, which is the maximum daily amount [bullet] with other drugs containing acetaminophen [bullet] 3 or more alcoholic drinks every day while using this product.
>
> Do not use with any other drug containing acetaminophen (prescription or

[77] 71 Fed. Reg. 77314-15 (Dec. 26, 2006).

[78] 74 Fed. Reg. 19385 (Apr. 29, 2009).

[79] The "Final Rule" also covered organ-specific warnings for other analgesics/pain relievers. See 74 Fed. Reg. 19385 (Apr. 29, 2009)("The [FDA] is issuing this final rule to require important new organ-specific warnings and related labeling for over-the-counter (OTC) internal analgesic, antipyretic, and antirheumatic (IAAA) drug products.").

[80] 74 Fed. Reg. 19385 (Apr. 29, 2009). See also Lee, W.M., Acetaminophen Toxicity: Changing Perceptions on a Social/Medical Issue, Hepatology 46(4): 966-970 (2007)(Pl. Ex. 9)(explaining the history of the 2009 Rule).

[81] 21 C.F.R. § 201.326 (Def. Ex. G, Doc. No. 49-7). The defendants argue that this "Final Rule" somehow serves as a finalization of the monograph or partial approval of the TFM. I do not read this FDA action in that way. From the information presented, the monograph system and the rulemaking system used by the FDA are similar in that both require a proposal for a rule or monograph, a period for comment or information gathering, and then a final determination. However, they are not the same process and are governed by different statutory provisions. A "final rule" on what is required at this time on a drug label is not the same as approving a monograph establishing under what conditions a drug may safely be taken OTC.

> nonprescription). If you are not sure whether a drug contains acetaminophen, ask a doctor or pharmacist.[82]

The rule requires that the liver warning be the first warning under the "Warnings" heading for the label.[83]

During the notice and comment period for the 2009 Final Rule, the FDA considered whether to add a warning about the adverse effects acetaminophen may have on persons who are fasting or malnourished. The FDA declined to adopt a "fasting" warning because it did not find sufficient evidence was presented to support such a requirement.[84]

The new liver warnings were required to be on all products by April 29, 2010. 74 Fed. Reg. 19385 (Apr. 29, 2009). Following the implementation of the 2009 Final Rule, McNeil changed the Extra Strength Tylenol label to include the following warnings:

> Liver warning: This product contains acetaminophen. Severe liver damage may occur if you take more than 8 caplets in 24 hours . . . with other drugs containing acetaminophen, [or] 3 or more alcoholic drinks every day while using this product.
>
> Do not use with any other drug containing acetaminophen (prescription or nonprescription)…
>
> Overdose warning: Taking more than the recommended dose (overdose) may cause liver damage.
>
> Do not take more than directed (see overdose warning).[85]

---

[82] 21 C.F.R. § 201.326(a)(iii)(A)-(B)(Def. Ex. G, Doc. No. 49-7).

[83] 21 C.F.R. § 201.326(a)(iii)(A)-(B)(Def. Ex. G, Doc. No. 49-7).

[84] 74 Fed. Reg. 19385, 19397-98 (Apr. 29, 2009). See also FDA Safety Analysis Power Point, Sept. 19, 2002 (Pl. Ex. 11)(explaining that "information [about fasting or malnutrition] often not captured" in AERs).

[85] 2010 Extra Strength Tylenol label (Hewes Decl. at Ex. 8)(Def. Ex. F, Doc. No. 49-6).

The previous label included the following warnings:

"Acetaminophen may cause liver damage," "Do not use with any other product containing acetaminophen," "Overdose warning: taking more than the recommended dose (overdose) may cause liver damage," and "do not take more than directed (see overdose warning)."[86]

II. OVERVIEW OF PLAINTIFF'S CLAIMS

a. FACTS REGARDING DENICE HAYES'S DEATH

Plaintiff Rana Terry brings this wrongful death and products liability action on behalf of her deceased sister's estate.[87] Her sister Denice Hayes died on August 31, 2010.[88] Denice was a single woman living with another sister Rebecca Hayes; the two had lived together for most of her life, up until the time of Denice's death.[89] Denice was not working at the time of her death due to health problems. Prior to leaving the workforce in 2008 for health reasons, she was employed as a teacher for several years.[90]

Denice's medical history included weight issues, back and leg pain, high blood pressure, and type II diabetes.[91] Denice had taken Extra Strength Tylenol periodically for

[86] 2009 Extra Strength Tylenol label (Hewes Decl. at Ex. 9)(Def. Ex. F, Doc. No. 49-6).

[87] See Plaintiff's Fact Sheet (Def. Ex. G, Doc. No. 49-8).

[88] See Plaintiff's Fact Sheet (Def. Ex. G, Doc. No. 49-8).

[89] See R. Hayes Dep. at 191.

[90] See Plaintiff's Fact Sheet (Def. Ex. G, Doc. No. 49-8).

[91] R. Hayes Dep. at 201.

years to treat some of these health conditions with no adverse effects.[92] She allegedly preferred Extra Strength Tylenol to Regular Strength Tylenol.[93] Rebecca typically did the shopping for both she and her sister. Rebecca was unaware of the difference between Extra Strength Tylenol's dosage and that of Regular Strength Tylenol.[94] However, she purchased Tylenol over its generic version because she and her sister thought Tylenol was a better, safer product.[95] The two sisters often watched television together and viewed ads for Tylenol.[96] According to Rebecca, Denice believed Tylenol was easier on the stomach based on advertising about the product.[97]

In August 2009, Denice underwent gastric bypass surgery to rectify her ongoing health problems.[98] After the surgery, she lost 180 pounds; she was able to stop taking her medications for high blood pressure and diabetes.[99] She used painkillers less than before

[92] Defendants' Statement of Facts, Material Fact No. 3; Plaintiff's Response admitting this fact. R. Hayes Dep. at 120-23 (agreeing that Ms. Hayes used Tylenol without any adverse effects for pain relief for at least 20 years before her death because it was safe and did not upset her stomach). In addition, Dr. Rex Sherer, who performed Ms. Hayes's 2009 gastric bypass surgery, testified to Ms. Hayes's chronic use of acetaminophen without incident. See R. Sherer, M.D. Dep., Mar. 23, 2015 at 76 (Def. Ex. O). See also A. Anantharaju, M.D. Dep., Oct. 15, 2014 at 23-27, 28-30, 32, 37-39, 65-66, 71 (Def. Ex. P).

[93] See R. Hayes Dep. at 39. Rebecca Hayes' deposition transcription can be found at Defendants' Exhibit J (Doc. No. 49-10) and Plaintiff's Exhibit 1 (filed under seal).

[94] R Hayes Dep. at 114.

[95] R. Hayes Dep. at 127, 130.

[96] R. Hayes Dep. at 191-193, 199-200.

[97] R Hayes Dep. at 129-31.

[98] See R. Hayes Dep. at 50-53 (Def. Ex. I, Doc. No. 49-9)(explaining how decedent was about 400 pounds at time of surgery and over 200 pounds at time of death), 200-201.

[99] See R. Hayes Dep. at 201, 229; R. Sherer, M.D. Dep. at 74-75 (Def. Ex. O, Doc. No. 49-15)(explaining Denice's conditions post gastric surgery).

because her back and leg pain had lessened.[100] In June 2010, she then had a fall which exacerbated her back pain.[101]

In mid-August 2010, Denice underwent lumbar laminectomy surgery.[102] She was instructed by her doctor to take Regular Strength Tylenol in conjunction with Lorcet, a prescription drug containing acetaminophen, and was not to exceed four grams of acetaminophen in a 24-hour period.[103] Denice took Extra Strength Tylenol from August 12, 2010 to August 29, 2010 at "appropriate times and in appropriate amounts."[104] She allegedly took tablets from a medium-sized bottle Rebecca had purchased the previous August to treat Denice's gastric bypass surgery pain.[105] That bottle was shared by the two sisters during that year.[106] Denice allegedly used that bottle until it ran out. Rebecca purchased another bottle of Extra Strength Tylenol for her sister on August 28, 2010.[107]

---

[100] R. Hayes Dep. at 201, 229.

[101] R. Hayes Dep. at 201-202; R. Terry Dep. at 53 (Def. Ex. I, Doc. No. 49-9).

[102] See R. Hayes Dep. at 156-57.

[103] See R. Hayes Dep. 156-57, 159-160

[104] Short Form Compl., Doc. No. 28 at ¶10; Pl. Fact Sheet at 11-12 (redacted), Ex. H; Defendants' Statement of Facts, Material Fact No. 5; Plaintiff's Statement admitting this fact (as quoted from the plaintiff's complaint). However, plaintiff also admits that no fact witness has personal knowledge that Ms. Hayes took her Extra Strength Tylenol as directed. See Defendants' Statement of Material Facts, Material Fact No. 4; Plaintiff's Statement admitting this fact.

[105] R. Hayes Dep. at 189, 229. According to Rebecca, she had purchased a medium-sized bottle of about 100 to 120 caplets of Extra Strength Tylenol in August 2009. Id.

[106] R. Hayes Dep. at 122, 189.

[107] R. Hayes Dep. at 147, 230. According to Rebecca, Extra Strength Tylenol was all that was available; Regular Strength Tylenol was not being sold at the WalMart where she purchased the product. R. Hayes Dep. at 207. See also R. Terry Dep. at 38 (Def. Ex. I, Doc. No. 49-9).

After her surgery, Ms. Hayes also began taking Lorcet as instructed by her doctor. However, she allegedly stopped taking Lorcet at some point before her death because she didn't like its side effects.[108] She continued to only take Extra Strength Tylenol because she thought it was gentler on her stomach.[109]

Between August 12, 2010 and August 31, 2010, Denice was in and out of the hospital.[110] She was admitted to the hospital overnight on August 20, 2010 for "nausea, vomiting, and impending dehydration."[111] She was experiencing back and rectal pain.[112] She was released on August 23, 2010.[113] During the week of August 23, 2010, Denice continued to experience symptoms of nausea and vomiting.[114] She was having trouble eating solid foods.[115] She allegedly took three to four doses of Extra Strength Tylenol each day during that week.[116] During this timeframe, Denice was cared for by several members of her family.[117]

---

[108] See R. Hayes Dep. at 34-36, 60, 67, 203-205. Denice also was prescribed hydrocodone with acetaminophen which she took right after she was discharged from her back surgery on August 12, 2010. See R. Hayes Dep. at 156. At what point between August 12th and 29th Denice stopped taking Lorcet is in dispute.

[109] R. Hayes Dep. at 34-36, 60, 67, 203-205.

[110] See R. Terry Dep. at 38 (Def. Ex. I, Doc. No. 49-9); R. Hayes Dep. at 38-41.

[111] See R. Terry Dep. at 38; R. Hayes Dep. at 38-41, 58-61, 76, 162, 205.

[112] See R. Hayes Dep. at 38.

[113] See R. Hayes Dep. at 162-163.

[114] See R. Hayes Dep. at 56-57.

[115] See R. Hayes Dep. at 46, 56, 66-67, 237-238.

[116] R. Hayes Dep. at 209-210, 226-227.

[117] See R. Terry Dep. at 38-40 (Def. Ex. I, Doc. No. 49-9); R. Hayes Dep. at 34-35, 39-40, 46, 56-57, 74; Plaintiff's Fact Sheet (Def. Ex. G, Doc. No. 49-8).

Denice was again admitted to the hospital on August 29, 2010.[118] The doctor diagnosed her with acute liver failure "most likely [from] accidental Tylenol overuse" and treated her with the acetaminophen antidote.[119] Denice died in the hospital two days later. Her cause of death is listed as "liver failure" caused by "acetaminophen intoxication."[120]

b. PLAINTIFF'S CLAIMS

In January 2012, Ms. Terry filed suit against Johnson & Johnson and McNeil asserting, *inter alia*, a negligent failure-to-warn claim. According to the plaintiff, the defendants knew that Tylenol could cause liver damage at or just above the recommended dose, especially when a person has been fasting or malnourished. The plaintiff claims the defendants are liable for Denice's death because they failed to warn consumers about the risk of injury and/or death Tylenol could cause.

The defendants move for summary judgment, arguing that the plaintiff cannot offer sufficient evidence at trial to support her failure-to-warn claim. The defendants also argue that the plaintiff's failure-to-warn claim is impliedly preempted.[121]

---

[118] See R. Hayes Dep. at 38-41, 58-61, 76.

[119] R. Hayes Dep. at 76, 171.

[120] See Denice Hayes Death Certificate (Doc. No. 45, Ex. A).

[121] The defendants note that the plaintiff did not comply with the page limit in her response to this motion. While it is true that the plaintiff should have moved for leave to exceed the page limit, I will excuse this oversight because the plaintiff's lengthy response helps to frame the larger issues in this case in a cohesive manner. However, the plaintiff may not be excused from such an oversight in the future.

III. SUMMARY JUDGMENT STANDARD

Summary judgment is appropriate "if the movant shows that there is no genuine dispute as to any material fact and that the movant is entitled to judgment as a matter of law." FED. R. CIV. P. 56(a). A dispute is "genuine" when "a reasonable jury could return a verdict for the nonmoving party" based on the evidence in the record. Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 248 (1986). A factual dispute is "material" when it "might affect the outcome of the suit under the governing law." Id.

A party seeking summary judgment initially bears responsibility for informing the court of the basis for its motion and identifying those portions of the record that "it believes demonstrate the absence of a genuine issue of material fact." Celotex Corp. v. Catrett, 477 U.S. 317, 323 (1986). Where the non-moving party bears the burden of proof on a particular issue at trial, the moving party's initial Celotex burden can be met simply by demonstrating to the district court that "there is an absence of evidence to support the non-moving party's case." Id. at 325. After the moving party has met its initial burden, the adverse party's response must cite "particular parts of materials in the record, including depositions, documents, electronically stored information, affidavits or declarations, stipulations (including those made for purposes of the motion only), admissions, interrogatory answers, or other materials." FED. R. CIV. P. 56(c)(1). Summary judgment is therefore appropriate when the non-moving party fails to rebut by making a factual showing that is "sufficient to establish the existence of an element

essential to that party's case, and on which that party will bear the burden of proof at trial." Celotex, 477 U.S. at 322. [122]

Under Rule 56 of the Federal Rules of Civil Procedure, the court must draw "all justifiable inferences" in favor of the non-moving party. Anderson, 477 U.S. at 255. The court must decide "not whether . . . the evidence unmistakably favors one side or the other but whether a fair-minded jury could return a verdict for the plaintiff on the evidence presented." Id. at 252. If the non-moving party has produced more than a "mere scintilla of evidence" demonstrating a genuine issue of material fact, then the court may not credit the moving party's "version of events against the opponent, even if the quantity

[122] Alabama law governs the plaintiff's failure-to-warn claim. This standard is the same as the summary judgment standard found in Alabama law. Alabama law requires that "proof by substantial evidence shall be required to submit an issue of fact to the trier of the facts [for motions for summary judgment in all civil actions]."Ala.Code 1975 § 12-21-12. "'Substantial evidence' has been defined as 'evidence of such weight and quality that fair-minded persons in the exercise of impartial judgment can reasonably infer the existence of the fact sought to be proved.'" Mixon By and Through Mixon v. Houston County, 598 So.2d 1317, 1318 (Ala. 1992)(quoting West v. Founders Life Assurance Co. of Florida, 547 So.2d 870, 871 (Ala. 1989)).

The moving party has the burden to make a prima facie case that no genuine dispute of material fact exists. When the burden of proof at trial is on the non-moving party at the summary judgment stage—as is the case here—the moving party "may satisfy the Rule 56 burden of production either by submitting affirmative evidence that *negates an essential element* in the nonmovant's claim or, assuming discovery has been completed, by demonstrating to the trial court that the nonmovant's evidence is insufficient to establish an essential element of the nonmovant's claim." Verchot v. General Motors Corp., 812 So.2d 296, 300 (Ala. 2001)(quoting Ex parte General Motors Corp., 769 So.2d 903, 909 (Ala.1999)(citations and quotation marks omitted))(emphasis in original). The non-movant then has the burden to put forth sufficient evidence to prove each element of her claims. Id. This evidence is then considered in the light most favorable to the non-movant and all reasonable doubts resolved against the moving party. See id. In other words, if the plaintiff as the non-movant cannot produce sufficient evidence to show her claim could be successfully established at trial, the defendants are entitled to summary judgment. See Verchot v. General Motors Corp., 812 So.2d 296, 300 (Ala. 2001)("If the nonmovant cannot produce sufficient evidence to prove each element of its claim, the movant is entitled to a summary judgment, for a trial would be useless.")(citations and quotation marks omitted)).

This standard is slightly different than if the party moving for summary judgment is also the party with the burden of proof at trial. If the movant were the plaintiff, she would be expected to put forth "credible evidence" to support her motion. See Verchot v. General Motors Corp., 812 So.2d 296, 300 (Ala. 2001)("If the movant has the burden of proof at trial, the movant must support his motion with credible evidence, using any of the materials specified in Rule 56(c), [Ala.]R.Civ.P. ('pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits')."(citations and quotation marks omitted)).

of the [moving party's] evidence far outweighs that of its opponent." Big Apple BMW, Inc. v. BMW of N. Am., Inc., 974 F.2d 1358, 1363 (3d Cir. 1992).

IV. Plaintiff Has Offered Sufficient Evidence for Her Failure-To-Warn Claim

I previously determined that Alabama law governs all of the plaintiff's claims. See Choice of Law Decision, May 20, 2015 (Doc. No. 41, 42).

a. Alabama Products Liability Law (AEMLD)

Product liability cases in Alabama are governed by the Alabama Extended Manufacturer's Liability Doctrine (AEMLD). The AEMLD is a hybrid liability doctrine which follows the tenets of Restatement 402A but allows defendants to pursue traditional tort defenses like assumption of the risk, lack of causation, or contributory negligence. See Casrell v. Altec Indus., Inc., 335 So.2d 128, 131-34 (Ala.1976); Atkins v. Am. Motors Corp., 335 So.2d 134, 137-43 (Ala.1976).[123] The AEMLD may be applied to wrongful death cases. Casrell, 335 So.2d at 134; Atkins, 335 So.2d at 144. To establish liability under the AEMLD, a plaintiff must show:

> (1) he suffered injury or damages to himself or his property by one who sells a product in a defective condition unreasonably dangerous to the plaintiff as the ultimate user or consumer, if
>
> (a) the seller is engaged in the business of selling such a product, and
>
> (b) it is expected to and does reach the user or consumer without substantial change in the condition in which it is sold.
>
> (2) Showing these elements, the plaintiff has proved a prima facie case although

[123] See, e.g., Yamaha Motor Co., Ltd. v. Thornton, 579 So.2d 619, 624-25 (Ala. 1991).

> (a) the seller has exercised all possible care in the preparation and sale of his product, and
>
> (b) the user or consumer has not bought the product from, or entered into any contractual relation with, the seller.

Casrell, 335 So.2d at 132-33.

"Under the AEMLD, a manufacturer has the duty to design and manufacture a product that is reasonably safe for its intended purpose and use." Townsend v. Gen. Motors Corp., 642 So.2d 411, 415 (Ala. 1994). This does not mean that the manufacturer is expected to insure against all harm or "to produce an accident-proof or injury-proof product." Id. "Proof of an accident and injury is not in itself sufficient to establish liability under the AEMLD; a defect in the product must be affirmatively shown." Id. (citing Casrell, 335 So.2d 128; Atkins, 335 So.2d 134). See also Sears, Roebuck & Co. v. Haven Hills Farm, Inc., 395 So.2d 991, 994-95 (Ala. 1981); Thompson v. Lee, 439 So.2d 113, 115 (Ala. 1983); Brooks v. Colonial Chevrolet–Buick, Inc., 579 So.2d 1328, 1332 (Ala. 1991); Verchot v. Gen. Motors Corp., 812 So.2d 296, 301 (Ala. 2001).

Under the AEMLD, "the important factor is whether [the product] is safe or dangerous when the product is used as it was intended to be used. However, danger may be obviated by adequate warning." Yarbrough v. Sears, Roebuck and Co., 628 So.2d 478, 481 (Ala. 1993)(quoting Casrell, 335 So.2d at 133 (Ala.1976); Atkins, 335 So.2d 134 (quotation marks omitted)). When a drug manufacturer "has reason to anticipate that danger may result from a particular use, as where a drug is sold which is safe only in limited doses, [the manufacturer] may be required to give adequate warning of the danger...and a product sold without such warning is in a defective condition." Atkins, 335

So.2d at 147 (quoting Restatement 402A Comment as an appendix to its decision to adopt AEMLD); see id. at 143, n. 5 ("Although our holding modifies the Restatement's theory of strict liability, the Comment, in large measure, retains its utility; therefore, we attach the official Comment to s 402A as an appendix hereto."). "[A] seller is not required to warn with respect to products, or ingredients in them, which are only dangerous, or potentially so, when consumed in excessive quantity, or over a long period of time, when the danger, or potentiality of danger, is generally known and recognized." Id. at 148.

b. The Elements of a Failure-to-Warn Claim

To establish liability under the AEMLD, the plaintiff must show that her sister was injured by the defendants' product sold to her "in a defective condition unreasonably dangerous…as the ultimate user or consumer." Casrell, 335 So.2d at 132-33. "Showing these elements, the plaintiff has proved a prima facie case although [the defendants have] exercised all possible care in the preparation and sale of [their] product, and [the decedent had] not bought the product from, or entered into any contractual relation with, the seller." Id. Under the AEMLD, "[a] manufacturer is under a duty to warn users of the dangerous propensities of a product only when such products are dangerous when put to their intended use." Gurley By and Through Gurley v. Am. Honda Motor Co., Inc., 505 So.2d 358, 361 (Ala. 1987). Specifically, the plaintiff must show that the warning provided was defective or inadequate in order to establish this breach of duty. See Deere & Co. v. Grose, 586 So.2d 196, 198 (Ala. 1991).

i. Adequacy of Warning

The defendants argue that the plaintiff has not offered sufficient evidence to show that a different, more adequate warning would have prevented the decedent's death. To be adequate, a warning "need not be the best possible warning" nor "warn of every potential danger." Gurley, 505 So.2d at 361. But, the manufacturer does have a duty to warn of potential hazards of foreseeable misuse if the dangers of misuse are ones of which the general public is unaware. See Yarbrough, 628 So.2d at 481; Gurley, 505 So.2d at 361 ("The objective of placing a duty to warn on the manufacturer of a product is to acquaint the user with a danger of which he is not aware, and there is no duty to warn when the danger is obvious." (citation omitted)).

The plaintiff offers evidence that the label was inadequate.[124] The plaintiff offers several reasons why a jury could find the label was inadequate. First, the plaintiff points out that the Extra Strength Tylenol label, at the time of the decedent's death, recommended that consumers take two tablets every 4 to 6 hours. The TFM offered dosing instructions of two tablets every 6 hours. Under the defendants' dosing instructions, a consumer could potentially take more acetaminophen over a 24-hour period than was recommended by the TFM. The TFM is not a final rule; therefore, the defendants' dosing instruction would not be *per se* negligent. However, the defendants' decision to instruct consumers to take more acetaminophen than recommended by the

[124] See R. Hayes Dep. at 196-198, 208-209.

TFM, without also warning of the potential risk of taking too much, could lead a reasonable jury to find that Extra Strength Tylenol's label was inadequate.[125]

Second, the plaintiff argues that the Extra Strength Tylenol label was deficient because it did not disclose the risk of severe liver damage or death from taking Extra Strength Tylenol at or just above the recommended dose.[126] The plaintiff has offered evidence from her own experts that Tylenol may be unsafe at recommended dosage levels.[127] She also has offered testimony from the defendant's own experts that they recommend their patients take below the recommended daily dose of Tylenol and emphasize to patients to take no more than the maximum daily dose, though Tylenol is advertised as "safe and effective."[128]

Lastly, the plaintiff argues that the label did not warn consumers about the risk of liver damage to those who were fasting or malnourished. To support this argument, the

[125] Which warnings Denice may have viewed—the pre-2009 Final Rule warnings or the post-2009 Final Rule warnings—is a fact in dispute. However, these dosing instructions were offered on both labels.

[126] This argument would apply to the pre-2009 Final Rule label.

[127] See N. Kaplowitz Dep., Apr. 21, 2015 at 271-73 (Pl. Ex. 31)("Q: "…you limit your Tylenol recommendations to patients with liver injury to two gram maximum? A: Correct. Q: Why two grams? A: Because I think that people with liver disease can't tolerate an insult, and two grams is what I would consider to be -- I consider the – the literature to -- and my personal experience to be such that I don't think I've -- you know, it's exceedingly rare. There may be a couple of cases in the literature where somebody described patients who were taking two grams or less as having liver injury. But my feeling is that it's -- you know, it's not a dangerous dose for somebody with liver disease. Q: You're testifying in this lawsuit and in the prior case that four grams can put somebody into acute liver failure? A: Right….Q: So you're giving them two grams with people with liver injury? A: Yeah. And that's exactly why the FDA lowered the dose from four grams to three grams; the recommended dose."); N. Kaplowitz, M.D. Expert Report (May 5, 2014)(Pl. Ex. 37); L. Plunkett, M.D. Expert Report (May 2, 2014)(Pl. Ex. 38). See also Neil Kaplowitz, M.D., Acetaminophen Hepatoxicity: What Do We Know, What Don't We Know, and What Do We Do Next?, Hepatology, Jul. 2004 at 23-26 (Pl. Ex. 39); William Lee, Acetaminophen and the U.S. Acute Liver Failure Study Group: Lowering the Risks of Hepatic Failure, Hepatology, Vol. 40, No. 1, 6-9 (2004)(Pl. Ex. 40).

[128] See R. Brown Dep. at 72 (Apr. 30, 2015)(Pl. Ex. 32)("I tell them to take no more than six or eight regular-strength tablets in a day, knowing that they'll take more…It's neigh on 2 grams [daily]."); S. Flamm Dep. at 168-73 (May 5, 2015)(Pl. Ex. 33)(explaining why he only recommends that patients take a maximum of 3 or 4 grams of Tylenol a day but advises them that this is the upper limit on what should be taken because he recognizes the likely risk of patients taking too much).

plaintiff offers scientific evidence, as far back as the 1990s, to suggest that fasting may put a consumer of Tylenol more at risk of hepatotoxicity.[129] The 2009 Final Rule itself also indicated that those who are fasting or malnourished may have lower glutathione stores, putting them at possible risk of liver damage. See 2009 Final Rule, 74 Fed. Reg. 19385, 19397 (Apr. 29, 2009)("Malnourished individuals have been shown to have reduced glutathione levels (Refs. 37, 38, and 39). Therefore, it is possible that low glutathione levels may increase the risk for liver injury because there would be less available to bind to NAQPI. Low glutathione levels may [be] a surrogate for identifying a population at increased risk of liver injury with acetaminophen, but it was unclear how much of the deficiency is necessary."). Drawing all inferences in the light most favorable to the plaintiff, a reasonable jury could find that the defendants did not adequately warn of this risk as well.

Even if Denice did take more than the recommended dose, this error would not necessarily defeat the plaintiff's claim. "[P]roof that a product was used as intended is not an element of a prima facie case under the AEMLD." Sears, Roebuck and Co. v. Harris, 630 So.2d 1018, 1028 (Ala. 1993). Instead, "a user's misuse of an allegedly defective product is an affirmative defense to liability under the AEMLD, which the defendant must plead and prove." Id. (citing Kelly v. M. Trigg Enters., Inc., 605 So.2d 1185, 1192 (Ala. 1992)). "Where a warning has been provided, a question arises as to whether the

[129] See Whitcomb & Block, Association of Acetaminophen Hepatotoxicity with Fasting and Ethanol Use, 272 JAMA 23, 1845-1850 (1994)(Pl. Ex. 12)("This study suggests that fasting may be an important predisposing factor for acetaminophen hepatotoxicity in patients taking 4 to 10 g of acetaminophen within 24 hours."). See also C. Blume Dep. at 106-109 (Def. Ex. N, Doc. No. 49-14)(explaining how concerns about effect of fasting or malnutrition have been noted in scholarly articles).

warning was adequate, and adequacy of the warning is a question of fact for the jury." Brasher v. Sandoz Pharm. Corp., Nos. CV–98–TMP–2648–S, CV–98–TMP–2650–S, 2001 WL 36403362, at *13 (N.D. Ala. Sept. 21, 2001)(citing Toole v. McClintock, 999 F.2d 1430, 1433 (11th Cir. 1993)).[130]

The plaintiff offers evidence that even if Denice took more than the recommended dose, this error was foreseeable. There is evidence that the defendants were well aware that consumers often unintentionally took too much Tylenol, leading to liver damage. See, e.g, Summary of Studies Examining Consumer Use of Acetaminophen at 2 (Pl. Ex. 34)(offering evidence from 2000s, including survey conducted by McNeil itself, that upwards of half of acetaminophen users misuse or take more than the recommended dose). This was a topic of concern in the medical community for several years before Denice died. In addition, the plaintiff argues that the information presented by the defendants about the risks of Tylenol—both on the label and in advertisements—would lead a reasonable consumer to be unaware that acute liver failure or death was a possible result of taking too much Tylenol over a short period of time.[131] From what has been

[130] See also CDER Working Group Executive Summary and Recommendations, Feb. 26, 2008 (Pl. Ex. 8) (explaining how unintentional overdose could be the result of many different factors)("[W]hen someone takes an amount greater than labeled, it is unclear whether it is a case of failing to read the directions, failing to understand the directions, failing to understand that severe liver injury can result from not following the directions or failing to realize that more than one of the medications used contained acetaminophen.").

[131] See also R. Hayes Dep. at 198-199, 212-214, 216-217; CDER Working Group Executive Summary and Recommendations, Feb. 26, 2008 (Pl. Ex. 8)("Current warnings of overdose and labeling identifying products containing acetaminophen have not adequately decreased the number of serious cases of liver injury.").

provided, a reasonable jury could find that the Tylenol label did not adequately warn consumers of the risk of taking Tylenol at or just above the recommended dose.[132]

The plaintiff also offers evidence that an adequate label would have prevented Denice's death. The plaintiff's cause of death is listed as acetaminophen-induced liver failure.[133] She was treated in the hospital before she died for this condition. The plaintiff offers an expert report from Timothy Davern, II, M.D. who has studied ALF for many years. See Expert Report of T. Davern M.D. (Pl. Ex. 20). Dr. Davern points to parts of Denice's medical record which show she was not experiencing liver or renal problems

---

[132] A reasonable jury may infer that the label was inadequate given that Tylenol is an OTC drug which is perceived and advertised as being safe to take. See CDER Working Group Executive Summary and Recommendations, Feb. 26, 2008 (Pl. Ex. 8)("Consumers perceive that OTC products are extremely safe and not likely to lead to serious toxicity. The marketing of OTC products emphasizes their safety and this perception may be reinforced by the availability of package sizes with large numbers of pills."); Lee, W.M., Acetaminophen Toxicity: Changing Perceptions on a Social/Medical Issue, Hepatology 46(4): 966-970 (2007)(Pl. Ex. 9)(explaining that advertisements tout the drug as "safest"). A reasonable jury may also conclude that the label did not adequately warn of the seriousness of possible side effects resulting from overdose. See CDER Working Group Executive Summary and Recommendations, Feb. 26, 2008 (Pl. Ex. 8)("Consumers are not aware that acetaminophen can cause serious liver injury, in part because product labels do not adequately warn of this problem.").

OTC advertising is not required to list possible side effects or active ingredients of advertised drugs. See Ellen Frank, Director, Div. of Public Affairs, CDER of the FDA, Powerpoint, Jun. 29, 2009 at 179 (Pl. Ex. 21). However, Ashley McEvoy, a McNeil executive, testified that advertising is one way that McNeil uses to "educate" consumers about McNeil's products. See A. McEvoy Dep., Feb. 12, 2014 at 283-86 (Pl. Ex. 35).

[133] The defendants argue that expert testimony is required to show causation. Ordinarily, expert testimony is required when the nature of the defect is complex or technical. See Sears, Roebuck & Co. v. Haven Hills Farm, Inc., 395 So.2d 991, 995 (Ala. 1981); Brooks v. Colonial Chevrolet–Buick, Inc., 579 So.2d 1328, 1332 (Ala. 1991). "This does not mean, however, that experts are always required, but simply that they are usually essential to produce evidence from which lay jurors may reasonably infer that the defective condition of the product is the cause of the product's failure and plaintiff's resultant injury." Haven Hills Farm, Inc., 395 So.2d at 995. If a jury could draw such an inference without expert testimony, "a prima facie case is nonetheless established." Id. See also Brooks, 579 So.2d at 1332.

In this case, expert testimony may help a jury understand Denice's cause of death. However, Denice's medical records have consistently indicated that acetaminophen-induced acute liver failure was the reason she was hospitalized before she died. The death certificate listed this as her cause of death. Under the circumstances provided, causation may not be as complex as the defendants make it out to be. What the plaintiff has provided regarding causation is sufficient for this motion. At trial, the plaintiff will have to establish the plaintiff's cause of death through testimony. The defendants can then offer expert testimony to rebut what Denice's doctor determined.

prior to June 2010. See Expert Report of T. Davern M.D. (Pl. Ex. 20)(discussing how Ms. Hayes' liver was "normal in size" at the time of her gastric bypass surgery in August 2009 and how a colonoscopy in June 2010 produced benign results). After reviewing her medical history, he concluded that Denice's ALF "was caused by acetaminophen poisoning related to Tylenol ingestion for therapeutic purposes." Expert Report of T. Davern M.D. (Pl. Ex. 20).

In addition, Rebecca testified she would not have purchased Extra Strength Tylenol if she were aware of the risks of liver failure and death.[134] The plaintiff offers evidence that Denice, who was not a risk taker, stopped taking Lorcet because she was concerned about its side effects.[135] Drawing all inferences in the light most favorable to the plaintiff, a reasonable jury could find that the defendants breached their duty to warn of known risks of Extra Strength Tylenol, making the label inadequate. Furthermore, a jury could find that an adequate label would have prevented Denice's death.

ii. Proof for Causation: Read and Heeded

To prove causation, the plaintiff will also have to show at trial that Denice would have read and heeded an adequate warning and that an adequate warning would have prevented the decedent's death.[136] See Yarbrough v. Sears, Roebuck and Co., 628 So.2d 478, 482 (Ala. 1993)("A negligent-failure-to-adequately warn case cannot be submitted to a jury unless there is some evidence that the allegedly inadequate warning would have

[134] See R. Hayes Dep. at 214, 217-219.

[135] See, e.g., R. Hayes Dep. at 34 and at 222-226 (Def. Ex. J, Doc. No. 49-10).

[136] As the parties agree, Alabama does not entitle the plaintiff to a "heeding" presumption.

been read and heeded and would have kept the accident from occurring." (quoting Gurley v. Am. Honda Motor Co., 505 So.2d 358, 361 (Ala. 1987)); Deere & Co. v. Grose, 586 So.2d 196, 198 (Ala. 1991)(same); Sears, Roebuck and Co. v. Harris, 630 So.2d 1018, 1030 (Ala. 1993). See also Brasher v. Sandoz Pharm. Corp., Nos. CV–98–TMP–2648–S, CV–98–TMP–2650–S, 2001 WL 36403362, at *13 (N.D. Ala. Sept. 21, 2001)("Under Alabama law, to prevail in a warnings claim, the plaintiffs also must demonstrate a causal link between the allegedly inadequate warning and the injury. In cases such as these, that means that the plaintiffs must demonstrate that, had the defendant given an adequate warning, it would have been read and heeded by the prescribing physicians."); Garrison v. Novartis Pharms. Corp., 30 F. Supp. 3d 1325, 1335-1337 (M.D. Ala. 2014); Barnhill v. Teva Pharms. USA, Inc., 819 F. Supp. 2d 1254, 1262 (S.D. Ala. 2011)(explaining that Alabama law does not presume that the plaintiff would have read and heeded an adequate warning).

The defendants argue that the plaintiff cannot offer evidence that Denice would have read and heeded the label's warnings. In response, the plaintiff has offered evidence that Denice followed warnings on labels. Her sisters testified in their depositions that Denice would read labels, not take medication which would harm her, and would follow doctor's instructions.[137] There is evidence in her medical record that Denice was generally compliant with her doctor's instructions.[138] Doctor's notes indicate Denice told her doctor she had taken her last dose of Tylenol the night before she was admitted to the

[137] See R. Hayes Dep. at 123, 125, 166, 210-211, 222-223.

[138] See R. Brown Dep., Apr. 30, 2015 at 284-87 (Pl. Ex. 32); S. Flamm Dep. at 262 (May 5, 2015)(Pl. Ex. 33).

hospital on August 29, 2010.[139] There is also no evidence to show that Denice was intentionally trying to commit suicide or overdose to harm herself.[140]

The defendants argue that there is no evidence that anyone actually saw Denice take the recommended dose of Tylenol or that she actually read and heeded the warnings on the label.[141] Denice was being cared for by several family members so no one person can verify the dosage she took.[142] However, the plaintiff plans to offer testimony by the decedent's sisters and doctors that she was compliant with her doctor's medical directions.[143] Denice's sister Rebecca lived with her for most of her life; she can speak to her sister's habits. This information is admissible under Federal Rule of Evidence 406. Whether this information about habit is credible is for a jury to decide.

Drawing all inferences in the light most favorable to the plaintiff, a reasonable jury could find that Denice would have read and heeded adequate warnings. Viewing the facts in the light most favorable to the plaintiff, a reasonable jury could find that the Extra Strength Tylenol label did not adequately warn of acute liver failure and possible death. It

[139] See R. Hayes Dep. at 170-171. According to Rebecca's testimony, she saw Denice take 2 caplets at bedtime. She knew Denice had gotten up during the night and "might" have taken more caplets. Id.

[140] See R. Brown Dep., Apr. 30, 2015 at 285-87 (Pl. Ex. 32); S. Flamm Dep., May 5, 2015 at 260, 262 (Pl. Ex. 33).

[141] See R. Hayes Dep. at 34-36 (Def. Ex. J, Doc. No. 49-10). The defendants rebut this evidence but pointing to information contained in decedent's life insurance proceedings. The information indicates that Denice "overdosed" on Tylenol. Whether that information can be presented at trial will be determined by a pending motion in limine. Even if the information can be presented, its mere existence does not negate the other evidence put forth that the decedent had taken the recommended dose. These competing pieces of evidence create a genuine dispute of material fact about whether the plaintiff would have read and heeded a different warning.

[142] See R. Terry Dep. at 38-40 (Def. Ex. I, Doc. No. 49-9).

[143] See, e.g., R. Terry Dep. at 38 (Def. Ex. I, Doc. No. 49-9).

is for a jury to decide if the Tylenol label adequately advised users of known risks of Tylenol.

V. Genuine Disputes of Material Fact Exist

The parties agree on all material facts except two. These two disputes are genuine and require this case to proceed before a jury.

a. Regarding the Label

First, the parties dispute which label was on the bottle of Extra Strength Tylenol used by Denice before she died. The plaintiff contends the bottle was purchased in August 2009. The defendants claim the bottle was purchased in August 2010.[144] This dispute is material because the label on Extra Strength Tylenol changed in early 2010. The new label added one word but that word is important. While the old label warned that an overdose of Extra Strength Tylenol could cause liver damage, the new label warned that an overdose could cause "severe" liver damage. If Denice relied on the warnings in the 2009 label, a reasonable jury could find that the lack of the warning of "severe" liver damage could have made that label inadequate.

While cleaning out Denice's belongings after her death, Denice's sisters discarded both the bottle of Extra Strength Tylenol and the bottle of Lorcet.[145] According to

[144] There is also evidence that Denice may have taken Tylenol from bottles with different labels.

[145] Pl. Fact Sheet at 13, ¶8; R. Terry Dep. at 41, 61-62, 176-179 (Def. Ex. I, Doc. No. 49-9)(confirming her sister threw away vitamins, stomach medicines, Tylenol, as well as Lorcet, a prescription product containing acetaminophen).

The defendants implicitly argue in their reply brief that I should only allow the 2010 label to be considered as evidence because the plaintiff failed to preserve the Tylenol bottle. Sanctioning the plaintiff in this way appears unwarranted. There is no evidence that the plaintiff's disposal of the bottle was meant to be spoliation of evidence.

Rebecca, she had purchased a medium-sized bottle of about 100 to 120 caplets of Extra Strength Tylenol in August 2009.[146] That bottle was shared by the two sisters during the following year.[147] Denice allegedly used that bottle in August 2010 until it ran out. Rebecca purchased another bottle of Extra Strength Tylenol for her sister on August 28, 2010.[148] Denice may have taken doses from this bottle before going to bed. She then was taken to the hospital the next morning.

Which warning Denice viewed is a question for the jury to answer. A jury will need to make credibility determinations about the family members' rendering of Denice's final days to answer this question. For this reason, this dispute is genuine and must be decided by a jury.

b. Regarding the Cause of Death

The parties also dispute Denice's cause of death. The plaintiff, relying on Denice's medical records from doctors treating her before her death and on expert opinions, cite acetaminophen-induced acute liver failure as the cause of death.[149] The defendants, relying on experts who reviewed Denice's medical records, claim that Denice died from

---

From all that has been provided, it is more likely that one of Ms. Hayes' sisters disposed of the bottle while going through her belongings, long before considering a wrongful death suit.

[146] R. Hayes Dep. at 189, 229.

[147] R. Hayes Dep. at 122, 189.

[148] R. Hayes Dep. at 147, 230. According to Rebecca, Extra Strength Tylenol was all that was available; Regular Strength Tylenol was not being sold at the WalMart where she purchased the product. R. Hayes Dep. at 207. See also R. Terry Dep. at 38 (Def. Ex. I, Doc. No. 49-9).

[149] See Supplement of Timothy Davern, M.D. Expert report (Pl. Ex. 29)(rebutting the defendant's conclusion that sepsis was the cause of death).

multi-system organ failure likely caused by sepsis. What caused the decedent's death is a genuine dispute of material fact. This alone defeats summary judgment.

VI. The Plaintiff's Claims are Not Impliedly Preempted

The defendants also argue that the plaintiff's claims are preempted "under implied conflict principles."[150]

a. Implied Preemption

Preemption is a concept based on the Supremacy Clause of the U.S. Constitution that provides a conflicting state law will be trumped by its federal counterpart. See Mut. Pharm. Co. v. Bartlett, 133 S. Ct. 2466, 2472-73 (2013)(citing U.S. Const., Art. VI, cl. 2). Even if a federal statute does not expressly preempt a state law, the state law may be impliedly preempted where it is "impossible for a private party to comply with both state and federal requirements." Id. at 2473 (quoting English v. Gen. Elec. Co., 496 U.S. 72, 79 (1990)(quotation marks omitted)).[151] There is a general presumption against preemption. See, e.g., Deweese v. Nat'l R.R. Passenger Corp. (Amtrak), 590 F.3d 239, 246 (3d Cir. 2009)(citing Cipollone v. Liggett Group, Inc., 505 U.S. 504, 516 (1992)).

[150] The Supreme Court has identified three types of preemption: express, field, and implied. Deweese v. Nat'l R.R. Passenger Corp. (Amtrak), 590 F.3d 239, 245 (3d Cir. 2009)(citations omitted). State law claims are expressly preempted if Congress indicates that conflicting state law will be trumped by the federal statute. See, e.g., 21 U.S.C. § 379r(e)(providing express preemption for certain regulations of non-prescription drugs). Field preemption "occurs when a state law impinges upon a 'field reserved for federal regulation.'" Deweese, 590 F.3d at 246 (quoting United States v. Locke, 529 U.S. 89 (2000)). The defendants only argue that preemption is implied. They concede that the plaintiff's claims would not be preempted under the other two theories. See also 21 U.S.C. §379(r)(e)(FDCA's savings clause exempting failure to warn cases from preemption).

[151] See also Deweese v. Nat'l R.R. Passenger Corp. (Amtrak), 590 F.3d 239, 246 (3d Cir. 2009)("[I]mplied conflict preemption exists when, 'under the circumstances of [a] particular case, [the state law] stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress.'")(quoting Hines v. Davidowitz, 312 U.S. 52, 67 (1941)); Florida Lime & Avocado Growers, Inc. v. Paul, 373 U.S. 132, 142–143 (1963)("A holding of federal exclusion of state law is inescapable and requires no inquiry into congressional design where compliance with both federal and state regulations is a physical impossibility for one engaged in interstate commerce…" (citation omitted)).

"Impossibility pre-emption is a demanding defense." Wyeth v. Levine, 555 U.S. 555, 573 (2009). The Third Circuit has cautioned against "lightly infer[ring]" preemption where "state compensatory regimes have traditionally played an important role." Fellner v. Tri-Union Seafoods, L.L.C., 539 F.3d 237, 249 (3d Cir. 2008). Whenever possible, preemption analysis should attempt to reconcile the state law and federal law with one another. See Deweese, 590 F.3d at 248. "[S]tate tort law and other similar state remedial actions are often deemed complementary to federal regulatory regimes" and fall "squarely within the realm of traditional state regulation." Fellner, 539 F.3d at 248-49.

b. The 2009 Final Rule and Wyeth v. Levine

The defendants argue that they were preempted from adding a "fasting" or "malnourishment" warning because the 2009 Final Rule did not include such a warning. McNeil argues that it "cannot unilaterally supplement or change its label with language inconsistent with the 2009 Final Rule." Defendants' Statement of Material Facts, Doc. No. 49-31 at ¶ 43. See also Jones Decl. at ¶¶ 58-59. This argument assumes that Ms. Hayes read the 2010 label—which included the 2009 Final Rule warnings—and not the 2009 pre-Final Rule label. Which label Ms. Hayes viewed is a question for the jury to answer.

Even assuming that Ms. Hayes viewed the post-Final Rule label warnings, the defendants' preemption argument fails. The Supreme Court rejected a similar argument in Wyeth v. Levine, 555 U.S. 555 (2009). Wyeth argued that it could not comply with both state and federal law because the FDA's approval process required it to use the exact text on a proposed drug label. Id. at 567. The Supreme Court explained that reliance on

this approved text was not enough for Wyeth to escape liability for a deficient label. Id. "[I]t has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times." Id. at 570-71. Brand-name drug manufacturers are "charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market." Id. at 571 (citing 21 CFR § 201.80(e), § 314.80(b); 73 Fed. Reg. 49605).

Specifically, the Supreme Court found that FDA regulations offer drug manufacturers a process by which to change their drug labels without using the formal administrative rulemaking process. Id. at 566. "[T]his 'changes being effected' (CBE) regulation provides that if a manufacturer is changing a label to 'add or strengthen a contraindication, warning, precaution, or adverse reaction' or to 'add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product,' it may make the labeling change upon filing its supplemental application with the FDA; it need not wait for FDA approval. §§ 314.70(c)(6)(iii) (A), (C)." Id. at 568. "[A]bsent clear evidence that the FDA would not have approved a change to [the drug's] label, we will not conclude that it was impossible for Wyeth to comply with both federal and state requirements." Id. at 571.

The Supreme Court opined in dicta that a failure-to-warn claim may be preempted if a drug manufacturer submitted a CBE change and the FDA rejected it. Id. at 571. The defendants focus on this language, claiming that the FDA's exclusion of a "fasting" or "malnourishment" warning in the 2009 Final Rule indicates a rejection of such a warning

and is analogous to the Court's hypothetical. I do not interpret the FDA's actions as the defendants do.

The 2009 Final Rule explained that the FDA only received three submissions regarding the fasting warning. See 74 Fed. Reg. 19397 (Apr. 29, 2009). The FDA could not "make a conclusion about the risk of liver injury due to acetaminophen in malnourished individuals." Id. The 2009 Rule did not require a fasting warning but stated the FDA would reconsider that position if new data became available. Id.[152] To decline to add a warning because public comments did not offer sufficient scientific evidence is a vastly different proposition than the FDA rejecting a warning because it is scientifically inaccurate, flawed, or confusing.[153] The FDA's decision is far from "clear evidence" in itself that the FDA would not approve a label change if McNeil offered evidence that it was warranted.[154] See Wolfe v. McNeil, 773 F. Supp. 2d 561, 568-69 (E.D. Pa.

[152] The FDA took similar actions when promulgating the TFM. The agency declined at that time to include an alcohol warning because the proposed evidence was "conflicting and insufficient." 53 C.F.R. 46218 (Nov. 16, 1988). Nonetheless, the defendants were later held liable for not including such a warning. See, e.g., Benedi v. McNeil P.P.C., Inc., 66 F.3d 1378, 1382 (4th Cir. 1995)("Benedi filed suit against McNeil in March 1994, and the case went to the jury on theories of breach of implied warranty and negligent failure to warn. After a three-day trial, the jury awarded Benedi $7,850,000 in compensatory damages and $1,000,000 in punitive damages."). McNeil also voluntarily added an alcohol warning, despite the FDA's previous decision to not require one. See McNeil CBE Letter to FDA, Jun. 16 1994 (Pl. Ex. D attached to Ex. 3 (Affidavit of Gerald Rachanow, Esq.)). The FDA then required that a warning about alcohol be added. See 63 Fed. Reg. 56789-02 (Oct. 23, 1998)("In the preamble to the proposed rule of this current rulemaking [i.e., the TFM], the agency addressed concerns raised in the 1988 proceeding about the need for a warning on the increased risk of liver toxicity when acetaminophen is taken with substances or drugs that induce microsomal enzyme activity, i.e., alcohol, barbiturates, or prescription drugs for epilepsy (53 FR 46204 at 46217). The agency found that the available data did not provide a sufficient basis to require such a warning at that time.").

[153] In fact, McNeil did not suggest that the "fasting" warning be added. Instead, McNeil disputed the need for such a warning. This scenario is quite different than the hypothetical one posed by the Court in Wyeth.

[154] See Wyeth, 555 U.S. at 571 ("Of course, the FDA retains authority to reject labeling changes made pursuant to the CBE regulation in its review of the manufacturer's supplemental application, just as it retains such authority in reviewing all supplemental applications. But absent clear evidence that the FDA would not have approved a change to Phenergan's label, we will not conclude that it was impossible for Wyeth to comply with both federal and state requirements.").

2011)(finding that FDA's decision not to adopt a citizen's request for a warning was not clear evidence of preemption because the FDA indicated stronger warnings were needed but disapproved of the proposed language), *compared with*, Robinson v. McNeil Consumer Healthcare, 615 F.3d 861, 873 (7th Cir. 2010)(finding clear evidence that the FDA would not have approved a label change because the "FDA decided not to require such a warning because it would confuse rather than inform"); Dobbs v. Wyeth Pharms., 797 F. Supp. 2d 1264, 1276-80 (W.D. Okla. 2011)(finding implied preemption when the FDA had repeatedly rejected a proposed label alteration submitted by the drug manufacturer).[155]

c. No Clear Evidence That McNeil Was Prevented from Changing the Label

Furthermore McNeil's own actions show that it was not impossible for McNeil to change the Extra Strength label.[156] As Wyeth made clear, the onus has always been on McNeil to ensure its label accurately reflects the risks of Extra Strength Tylenol.[157] If

---

[155] See also Lofton v. McNeil Consumer & Specialty Pharms., 682 F. Supp. 2d 662, 676-77 (N.D. Tex. 2010)(finding that FDA's decide not to adopt citizen's request for a warning was not clear evidence of preemption based on the circumstances), *judgment aff'd on other grounds*, 672 F.3d 372, Prod. Liab. Rep. (CCH) ¶18790 (5th Cir. 2012); Reckis v. Johnson & Johnson, 28 N.E.3d 445, 455-61 (Mass. 2015)(same); Hunt v. McNeil Consumer Healthcare, 6 F. Supp. 3d 694, 698-704 (E.D. La. 2014)(same); Brown v. Johnson & Johnson, 64 F.Supp.3d 717, 721-22 (E.D. Pa. 2014)(finding that defendants failed to meet burden of showing clear evidence); Valdes v. Optimist Club of Suniland, Inc., 27 So. 3d 689, 690-91 (Fla. 3d DCA 2009)(finding no implied preemption regarding Tylenol Cold warnings), *review denied*, 43 So. 3d 44 (Fla. 2010) and *cert. denied*, 131 S. Ct. 1021, 178 L. Ed. 2d 829 (2011); *compared with*, In re Fosamax (Alendronate Sodium) Prods. Liab. Litig., 951 F. Supp. 2d 695, 703 (D. N.J. 2013)(finding preemption warranted because FDA rejected manufacturer's request to add stronger warnings).

[156] See Perry v. Novartis Pharma. Corp., 456 F.Supp.2d 678, 685 (E.D. Pa. 2006)("[I]t is more in keeping with the narrow scope of preemption to allow state law to require the addition of warnings so long as there has been no specific FDA determination as to the sufficiency of the scientific evidence to support a particular warning."); Knipe v. SmithKline Beecham, 583 F.Supp.2d 553, 579 (E.D. Pa. 2008)("Quite unlike the cases finding state failure to warn cases preempted due to the FDA's clear and considered position on the warning at issue, the FDA had not repeatedly and/or publicly stated its position as to this warning.").

McNeil had knowledge and notice that a "fasting" or "malnourishment" warning was needed to supplement or strengthen Extra Strength Tylenol's existing warnings, it could have made a CBE application.[158] See Wyeth, 555 U.S. at 573.

Nonetheless, the defendants argue that they could not have voluntarily changed the label on Extra Strength Tylenol because the CBE procedure is only available for drugs regulated by the NDA process. This argument is logical given that Extra Strength Tylenol was only governed by the monograph process, not the NDA process, at the time of the decedent's injury and death. The CBE procedure is affiliated with the NDA process, not the monograph process. See 21 C.F.R. § 314.70 ("Supplements and other changes to an approved application"); Wyeth, 555 U.S. at 578-79 (explaining the CBE process).

A close look at the history of Extra Strength Tylenol's label changes contradicts McNeil's argument. In 1994, McNeil petitioned the FDA to add an alcohol warning and a concomitant use warning (i.e., "Do not use with other products containing acetaminophen") to the Extra Strength Tylenol label; it used the CBE process in

---

[157] See also FDA Approval Letter (Hewes Decl. at Ex. 1)(Def. Ex. F, Doc. No. 49-6)(advising McNeil that even under the NDA it was expected to monitor and report on the safety and efficacy of Extra Strength Tylenol).

[158] The defendants offer several non-binding cases to support their argument. These cases are factually and/or legally distinguishable. They are not persuasive. See In re: Celexa and Lexapro Mktg. & Sales Pracs. Litig., 779 F.3d 34, 43 (1st Cir. 2015)(finding that a drug manufacturer was implied preempted from changing its drug label because the court found no new information would have supported a CBE application based on distinguishable facts and procedural history); Robinson v. McNeil Consumer Healthcare, 615 F.3d 861, 873 (7th Cir. 2010)(finding clear evidence that the FDA would not have approved a label change because the "FDA decided not to require such a warning because it would confuse rather than inform"); Dobbs v. Wyeth Pharms., 797 F. Supp. 2d 1264, 1276-80 (W.D. Okla. 2011)(finding implied preemption when the FDA had repeatedly rejected a proposed label alteration submitted by the drug manufacturer); In re Fosamax (Alendronate Sodium) Prods. Liab. Litig., 951 F. Supp. 2d 695, 703 (D. N.J. 2013)(finding preemption warranted because FDA rejected manufacturer's request to add stronger warnings); Sykes v. Glaxo-Smithkline, 484 F. Supp. 2d 289, 307-318 (E.D. Pa. 2007)(pre-Wyeth decision finding impliedly preemption by the Vaccine Act of failure to warn claims because "could not have altered the labeling without FDA approval [unlike the CBE procedure]; the additional labeling would have posed a threat to the federal regulatory objectives of the FDA")(Stengel, J.); Horne v. Novartis Pharms., 541 F. Supp. 2d 768, 781-82 (W.D. N.C. 2008)(pre-Wyeth decision finding that claims were preempted because the text of an additional warning would directly conflict with the warnings already approved by the FDA).

accordance with 21 C.F.R. § 314.70 for NDA 17-552.[159] In its request for this label revision, McNeil indicated that the label change would be incorporated in the labeling "for all of [its] acetaminophen containing products for adults distributed under the OTC drug monographs."[160]

In 1998, McNeil withdrew the NDA for Extra Strength Tylenol (NDA 17-552). When it made this withdrawal, McNeil indicated that it would "continue to submit acetaminophen Adverse Drug Experience reports under NDA 19-872."[161] NDA 19-872 is the application for Tylenol Extended Relief Caplets.[162]

In 2001, after petitioning the FDA, McNeil added a warning stating: "[t]aking more than the recommended dose (overdose) could cause serious health problems."[163] This CBE petition was made under NDA 19-872 for Tylenol Extended Relief formula. McNeil indicated it would include the new warning on Tylenol Arthritis Pain Extended Relief "as well as other Tylenol acetaminophen products that are distributed under the OTC drug monographs."[164] It reiterated this point again in its petition saying: "These

[159] See Pl. Ex. D attached to Ex. 3 (Affidavit of Gerald Rachanow, Esq.)(McNeil Letter to FDA, Jun. 16, 2011); Pl. Ex. 43; Doc. No. 49-28 at 42-55.

[160] Doc. No. 49-28 at 43 (6/16/1994 Letter from McNeil to Dr. Weintraub/FDA).

[161] See Doc. No. 49-28 at 68 (5/11/98 Letter withdrawing Extra Strength Tylenol NDA).

[162] See, e.g., Doc. No. 49-28 at 57.

[163] McNeil Letter to FDA, Nov. 29, 2001 (Hewes Decl. at Ex. 4)(Def. Ex. F, Doc. No. 49-6). See Defendants' Statement of Material Facts, Doc. No. 49-31 at ¶ 13.

[164] McNeil Letter to FDA, Nov. 29, 2001 (Hewes Decl. at Ex. 4)(Def. Ex. F, Doc. No. 49-6).

same changes will be made to all other Tylenol products distributed under the OTC monographs."[165]

In 2002, at an advisory committee meeting with the FDA discussing acetaminophen labeling and safety, McNeil sought to further strengthen its Tylenol labels by replacing "serious health problems" language with specific language warning of overdose and liver damage.[166] The FDA approved that change in 2003.[167] In 2004, McNeil introduced the stronger warning regarding overdose/organ-specific liver damage on all Tylenol products.[168] Despite the defendants' insistence that changing the Extra Strength Tylenol label would be impossible, they already have done it.[169]

---

[165] McNeil Letter to FDA, Nov. 29, 2001 (Hewes Decl. at Ex. 4)(Def. Ex. F, Doc. No. 49-6).

[166] McNeil Letter to FDA, Oct. 15, 2002 (Hewes Decl. at Ex. 5) (Def. Ex. F, Doc. No. 49-6). See Defendants' Statement of Material Facts, Doc. No. 49-31 at ¶ 14.

[167] FDA letter to McNeil approving the changes "for use as recommended in the agreed upon labeling text," May 28, 2003 (Hewes Decl. at Ex. 6)(Def. Ex. F, Doc. No. 49-6).

[168] See McNeil Letter to FDA, May 22, 2003 (Hewes Decl. at Ex. 7)(Def. Ex. F, Doc. No. 49-6) and attached label for Extra Strength Tylenol (including the approved CBE changes).

[169] After the decedent's death in 2011, McNeil voluntarily changed the label again on Extra Strength Tylenol. See Doctor Letter 2011 (regarding McNeil's voluntarily reduction in the maximum daily dosage of Extra Strength Tylenol)(Pl. Ex. 2). While this evidence would typically be excluded under the Federal Rules of Evidence as a subsequent remedial measure, this information can be used to rebut the defendants' defense of impossibility. See FED. R. EVID. 407.

McNeil also volunteered to change its label during the 2009 FDA Advisory Committee meeting, agreeing to implement "dose titration" instructions. See McNeil's Presentation to Joint Meeting of the Drug Safety and Risk Management Advisory Committee, Nonprescription Drugs Advisory Committee and the Anesthetic and Life Support Drugs Advisory Committee, Jun. 29-20, 2009, Powerpoint (Pl. Ex. 22); Statement of Edward Kuffner, M.D., McNeil's Vice President of OTC Medical Affairs and Clinical Research, at the 2009 Advisory Committee Meeting (Pl. Ex. 50)("McNeil is recommending changing the current dosing directions on both the 325-milligram and 500-milligram formulations, seen here on your left, from take two tablets every four to six hours while symptoms last, to the proposed directions shown on the right, take one tablet, and if pain or fever does not respond to one tablet, two tablets may be needed. This dose titration model is identical to the directions on the current over-the-counter ibuprofen label. This significant change will encourage patients to use the lowest effective dose and should, therefore, decrease overall acetaminophen exposure within the general population."). From the evidence provided, the FDA approved this change. See Correspondence from FDA to McNeil President, June 10, 2010 (Plaintiff's Ex. 51). Though these instructions were never implemented, McNeil has put forth no evidence that the FDA was the obstacle to making this change.

Furthermore, Extra Strength Tylenol was and still is regulated by the Tentative Final Monograph (TFM) which is only a proposed rule. See 21 C.F.R. §§ 310, 343, 369 at 42604 (TFM)(Pl. Ex. 48); FDA letter to McNeil, 11/17/11 (Pl. Ex. 4). As explained by the FDA itself: "Under a TFM, manufacturers market products at their own risk and are able to make voluntary adjustments taking into context the information presented in the proposed TFM."[170] See FDA letter to McNeil, 11/17/11 (Pl. Ex. 4).[171] If the defendants

---

[170] The defendants argue that Extra Strength Tylenol has been classified as "generally recognized as safe and effective" (GRASE) because it was assigned to Category I under the proposed rule. The defendants imply I should give this categorization some weight. During the initial step of the monograph process, the available OTC drug ingredients were recommended by the panel of experts to be a Category I: GRASE, Category II: not GRASE, or Category III: unclear if GRASE or not. See http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ucm118349.pdf; http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ucm317137.htm.

This categorization appears to be nothing more than that—a way to organize the available drug ingredients. Those ingredients found to not be GRASE were not permitted to continue through the monograph process. See 58 Fed. Reg. 27636 ("Status of Certain Additional Over-the-Counter Drug Category II and III Active Ingredients")(May 10, 1993)("As mentioned, no substantive comments or new data were submitted to support reclassification of any of these active ingredients to monograph status. Therefore, before a final rule on each respective drug category is published, the Commissioner has determined that these ingredients are not generally recognized as safe and effective and that any OTC drug product containing any of these active ingredients not be allowed to continue to be initially introduced or initially delivered for introduction into interstate commerce unless it is the subject of an approved application.").

The TFM is a proposed rule, not a final regulation. See TFM 21 C.F.R. 343 at 35346 ("Based upon the conclusions and recommendations of the Panel, the Commissioner *proposes, upon publication of the final regulation*…" (emphasis added)); 53 C.F.R. 46204 ("In order to conform to terminology used in the OTC drug review regulations (21 CFR 330.10), the present document is designated as a "tentative final monograph." Its legal status, however, is that of a proposed rule."). The inclusion of the categorization of acetaminophen as GRASE in the TFM would not be binding until a Final Monograph/Rule was promulgated. See FDA/CDER, Guidance for FDA Staff and Industry, Marketed Unapproved Drugs—Compliance Policy Guide, Sec. 440.100 Marketed New Drugs Without Approved NDAs or ANDAs, Sep. 19, 2011, at 13 ("Drugs marketed in accordance with a final monograph are considered to be generally recognized as safe and effective (GRAS/GRAE) and do not require FDA approval of a marketing application.")(Doc. 49-20)(Ex. C attached to J. Jones Report, Def. Ex. S).

I do not read this categorical assignment as any sort of approval of Extra Strength Tylenol's safety and efficacy in every situation by the FDA. The regulations which outline the monograph process are titled "Procedures for classifying OTC drugs as generally recognized as safe and effective and not misbranded, and for establishing monographs." 21 C.F.R. § 330.10. The monograph process itself is intended to determine under what conditions OTC drugs are GRASE. 21 C.F.R. § 330.10(a)(8). ("[T]he Commissioner shall publish in the Federal Register a final order containing a monograph establishing conditions under which a category of OTC drugs or a specific or specific OTC drugs are generally recognized as safe and effective and not misbranded."). See also Gerald Dal Pan, M.D., Director of Office of Surveillance and Epidemiology, CDER/FDA, Powerpoint, Jun. 29, 2009 at 19 (Pl. Ex. 21)(OTC Monograph …[bullet point] Establishes conditions for use for ingredients determined to be Generally

became aware of information that fasting and malnourishment posed a serious health risk to Tylenol consumers, the onus was on them to seek a label revision.[172] McNeil's own former Vice President and Chief Medical Officer Anthony Temple, M.D. admitted as much during his deposition.[173]

There is no clear evidence that the defendants could not comply with both state law tort principles and FDA regulations.[174] The plaintiff's claims are not impliedly preempted.

VII. CONCLUSION

For the foregoing reasons, I will deny the defendants' motion for summary judgment on the plaintiff's failure-to-warn claim.

An appropriate Order follows.

Recognized As Safe and Effective (e.g., dose, labeling, testing)"). Under what conditions the usage of acetaminophen would be GRASE remain open because a final monograph/rule was never issued.

Even if the TFM gave some implicit approval of acetaminophen as GRASE, Extra Strength Tylenol could not be considered GRASE because the defendants were marketing it with dosing instructions that did not conform to the TFM. Under either scenario, this categorization does little to change the legal analysis of this case.

[171] McNeil's Vice President of Regulatory Affairs Lynn Pawelski agreed that this interpretation of the regulatory framework was accurate. See L. Pawelski Dep., Feb. 28, 2014 at 114-116 (Pl. Ex. 44). See also McNeil letter to the FDA re: label change, Jan. 27, 1995 (Def. Ex. Q attached to Ex. S (Certification of Judith Jones, M.D., Ph.D.))("We believe that the language we are using in the Directions section of our labeling is acceptable since the issue has not yet been finalized in the final monograph for Internal Analgesic Products.").

[172] See also E. Kuffner Dep., March 18, 2011 at 8-10 (explaining what duties a drug manufacturer has when new risks come to light in post-market surveillance). The defendants argue that 21 C.F.R. § 201.326(a), (c) supports their argument that they could not change the label warnings without FDA approval. Section 201.326 is a codification of the 2009 Final Rule. See Def. Ex. G, Doc. No. 49-7.While it states that all OTC acetaminophen-based products must contain certain warnings, it does not state that those products cannot contain other warnings. The warnings contained in 21 C.F.R. § 201.326 are a floor, not a ceiling.

[173] See A. Temple, M.D. Dep., Mar. 20, 2014, at 194-95 (Pl. Ex. 45). Defense regulatory expert Judith Jones, M.D. also admitted the same. See J. Jones, M.D. Dep., May 5, 2015 at 201 (Pl. Ex. 46). See also J. Jones Dep. at p.106 (admitting that her opinions on FDA's control over labeling is inconsistent with what the United States Supreme Court has decided in Wyeth v. Levine, 129 S.Ct. 118, 555 U.S. 555, 570-71 (2009)).

[174] See Hutto v. McNeil-PPC, Inc., 79 So. 3d 1199, 1209-10 (La. App. 3 Cir. 2011)(finding the same regarding preemption argument for Children's Tylenol and failure-to-warn claim regarding risk of liver damage/failure).